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The Australian and New Zealand
JOURNAL OF SURGERY

Vol. XXII—No. 1 AUGUST, 1952.

PANCREATICO-DUODENAL RESECTION FOR CARCINOMA

By Julian Orm Smith and Grayton Brown
Royal Melbourne Hospital

THE credit for raising pancreatico-duodenal resection to the level of a legitimate surgical procedure must be granted to the surgeons of the United States of America, notably Halsted (1900), Coffey (1909), Whipple (1935), Brunschwig (1942), Cattell (1945) and Clagett (1946). However, it is not the purpose of this paper to consider or describe the industry of the men who were responsible for the increasing success which has been achieved in attacking these malignant tumours, but to record our own experiences, admittedly brief, in the hope that they may prove instructive. These experiences have produced two main impressions. First, that toxic or infectious hepatitis can usually be distinguished pre-operatively from obstructive jaundice; and secondly, that as a surgical consideration, carcinoma of the pancreas has a worse prognosis than carcinoma of the ampulla, for, although these tumours would appear to be allied from a regional aspect, the ampullary growths present with jaundice much earlier.

Diagnosis

The problem of distinguishing obstructive jaundice and infectious hepatitis is a pre-operative one. We were fortunate in that most of the patients in this series were fully investigated by our medical colleagues who studied the value of the biochemical tests of liver function, notably the cephalin flocculation test and the level of serum alkaline phosphatase, in the differential diagnoses of infectious hepatitis from obstructive jaundice (I. J. Wood *et alii* 1948 and 1949). Occasionally aspiration liver biopsy was of value. However, whenever the diagnosis was in doubt, laparotomy was considered essential. The early use of these biochemical tests would have avoided the delay in operating in our Case 7 who had been treated by his family physician for infectious hepatitis despite six months' jaundice. The physician was understandably misled by the patient's well-being and by fluctuations in the intensity of the jaundice, not a rare event in small growths of the ampulla.

In addition, these biochemical tests and liver biopsies lend weight to the clinical observation that these patients have a degree of liver damage due to obstruction and infection of the biliary passages. A preliminary decompression of the biliary system together with the administration of antibiotics, leads to gratifying improvement both in liver function and the general health of the patient. This, in our opinion, justifies a two stage operation.

Clinically the finding of a palpable gall bladder is significant of malignant disease and calls for laparotomy. Even if the gall bladder cannot be palpated but the history, biochemical tests or perhaps liver biopsy suggest obstruction, a laparotomy should be performed without delay. Silent stones, hydatid disease or carcinoma may be present and require operative removal.

Further diagnosis will be required when the abdomen is opened. A distended gall bladder at once suggests malignant obstruction. However, the diagnosis, even at this stage, may be quite a problem. Massive carcinoma of the head of the pancreas is easily recognized. A smaller tumour of the head or the ampulla is more difficult to diagnose accurately, especially if the pancreatic duct is obstructed with dilatation and infection behind this obstruction giving the false impression of massive malignancy. In less severe cases the surgeon, when placed in the awkward predicament of not being able to make a confident diagnosis even when the gland is under his eyes and fingers, may be aided by observing the following minor differences:

1. Deep jaundice with a tense gall bladder and vague or small induration felt through the duodenum is probably due to carcinoma.
2. Incomplete jaundice and a distended gall bladder (as opposed to tense) is more probably due to chronic pancreatitis.

Biopsy of the pancreas has not been of assistance in diagnosing malignancy in doubtful cases because the tumour tissue is difficult to locate; it has, however, been used by us for the investigation of cases of chronic relapsing pancreatitis.

TECHNIQUE OF OPERATION

If the diagnosis of a biliary obstruction due to a growth has been made, then the plan of attack must be definite. Our experience in this series is that is is rarely profitable to perform a radical resection for a moderately large carcinoma of the pancreas. The opinion of those with a much wider experience confirms this view. On the other hand it is apparent that every ampullary or small pancreatic growth should be resected because, now, the hazard of operation is reasonable in these cases and there is every chance of a much longer survival than when a palliative anastomosis alone is performed. For reasons given above, we are of the opinion that a two stage operation is preferable to one stage. Any technical embarrassments which the surgeon may suffer at the second operation are more than balanced by the advantages the patient enjoys in his well-being after the first stage and by his increased ability to withstand the resection which is carried out about one month later. Despite our strong feelings in this matter at the present time, we have to draw attention to the differing opinions of authorities such as Clagett (1946), who advocate the one stage operation, but we are encouraged in the knowledge that Cattell (1945) has a preference for spacing the decompression and resection.

First Stage.

Extensive manipulation or dissection to determine operability at the first stage is unwise as it interferes with the second stage dissection. The final decision on operability is determined at the second operation.

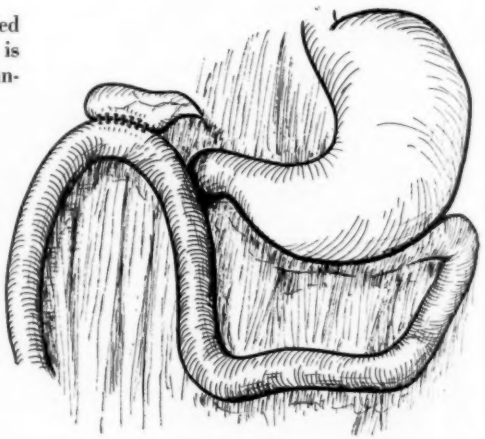

FIG. I. First Stage: Cholecystenterostomy with long afferent limb.

In four patients upon whom the resection has been performed in this series, cholecystjejunostomy has been the first stage operation (Fig. I). A cholecystostomy through a small lateral incision with a minimum of exploration was performed in one case, but we gained the impression that this patient did not improve as much as those who received their own bile into the alimentary canal. Osborn (1951) on the other hand, favours cholecystostomy as the first stage.

The anastomosis is made to the jejunum at least two feet from the duodeno-jejunal flexure, so that the difficulties of manipulation during the second stage may be reduced to a minimum. The incision which we have used is a right lateral oblique one placed rather further out than the classical Kocher.

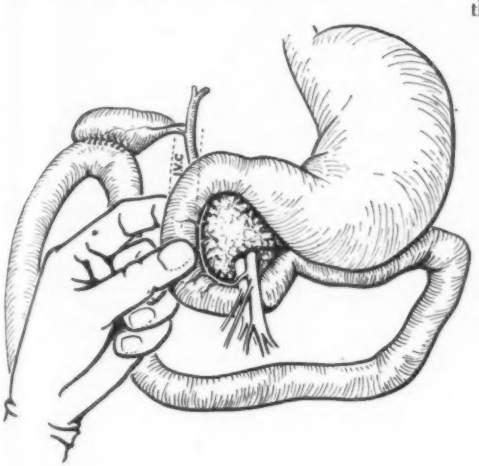

FIG. II. Second Stage. Operability in relation to inferior vena cava.

Second Stage.

The first actual resection in our series was performed by J.O.S. in 1946 on a man with carcinoma of the ampulla. He is still alive and well. Preceding this operation, some half dozen were performed on the cadaver in the post-mortem room, and we feel sure that this course should be pursued by anyone who is about to attempt the operation for the first time. Although our technique shows no major differences from most published descriptions and our numbers are small, we consider it would be of value to record our procedure in some detail and to relate our experiences.

The operation is best commenced with an intravenous infusion of 5 per cent. glucose running so that blood can be given later with the least disturbance. It is advisable to have four pints of blood available. A Ryle or Rehfuss tube is passed before operation. The most satisfactory anaesthesia is nitrous oxide or cyclo-propane, and curare.

On separate occasions, transverse and midline incisions have been used to open the abdomen. There appears to be no great advantage of the one over the other, as access to the region is not difficult.

The first step of the operation consists in examining for operability by mobilizing the duodenum, swinging it to the left to expose the inferior vena cava, and passing the finger between the growth and this vessel (Fig. II). This manoeuvre, except in advanced cases, is easily accomplished. Then the superior mesenteric vein is located and traced upwards to the neck of the pancreas while the portal vein is defined above. Fingers are now passed from above and below following the course of these veins (Fig. III). It is then possible to determine if the portal vein can be dissected free from the tumour; if this is impossible, it is useless to proceed.

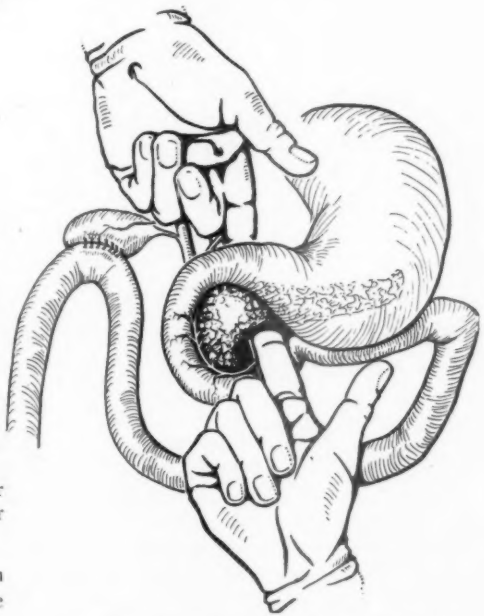

FIG. III. Operability in relation to portal vein and superior mesenteric vessels.

If it is decided that the growth is operable, the pylorus is divided between clamps and the proximal end mobilized by dividing parts of the greater and lesser omentum.

This allows the right gastric and gastro-duodenal arteries to be ligated, but only after the hepatic artery has been clearly identified (Fig. IV). This is an important point for, in Case 5, this large artery, being in an abnormal position, was mistaken for the gastro-duodenal artery and ligated with a fatal result. As part of this preliminary dissection, not only the hepatic artery but also the superior mesenteric and middle colic arteries should be plainly displayed so that the surgeon is continually aware of their exact position.

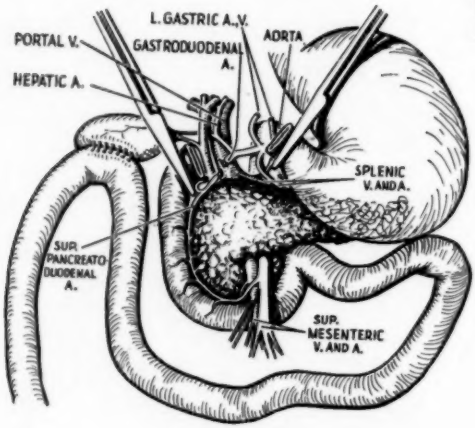

FIG. IV. Division of pylorus and ligation of gastro-duodenal vessels.

The neck of the pancreas is then divided between silk ligatures which act as temporary haemostats (Fig. V). The common bile duct and cystic duct are then identified, and the former ligated and divided below the entry of the latter into it. This stage of the operation is much more difficult than one would anticipate. The free border of the lesser sac, or gastro-hepatic omentum, contains more than the bile duct, hepatic artery and portal vein. There are lymphatics, lymph glands and minor vessels which together form quite a thick leash. An additional hazard is the frequency with which the cystic duct enters the common bile duct low down, close to the duodenum; thus, in Cases 3 and 6, the cystic duct was inadvertently divided along with the common bile duct necessitating a second anastomosis of the common bile duct to the jejunum. This is usually a tedious performance because the calibre of the duct by this time has been reduced by the first stage cholecystjejunostomy.

The third part of the duodenum is then drawn to the right from behind the superior mesenteric vessels, and, as the region of the duodeno-jejunal flexure is reached, is divided and oversewn (Fig. VI). The distal duodenum is on tension at this stage and the great tendency for the divided part to rebound must be anticipated by fixing it with Allis forceps before division.

It then remains for the surgeon to remove the pancreatico-duodenal mass by freeing the uncinate process from behind the superior mesenteric vein (Fig. VII). This is the most hazardous part of the operation owing to the many short, thin-walled veins which run direct from the pancreas into the superior mesenteric and

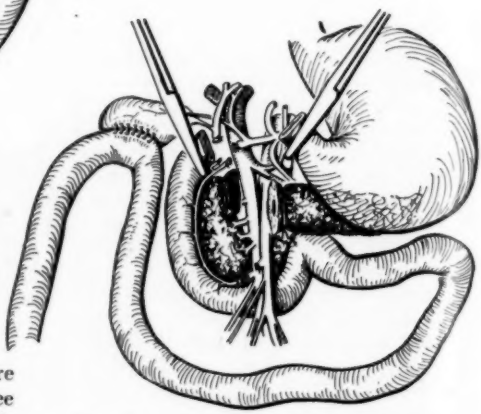

FIG. V. Division of neck of pancreas and common bile duct.

and portal veins on their right side. Each of these tributaries must be isolated, underrun with a small aneurysm needle holding fine silk, doubly ligated and then divided. We believe this to be a much safer method

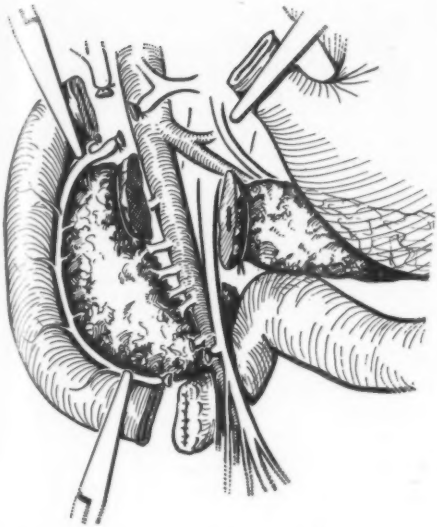

FIG. VI. Division of third part of duodenum.

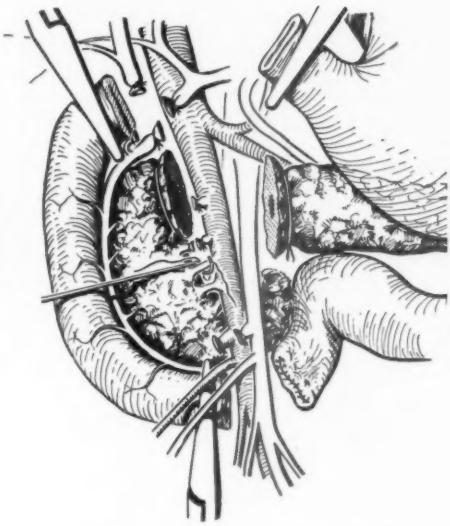

FIG. VII. Division of veins between ligatures.

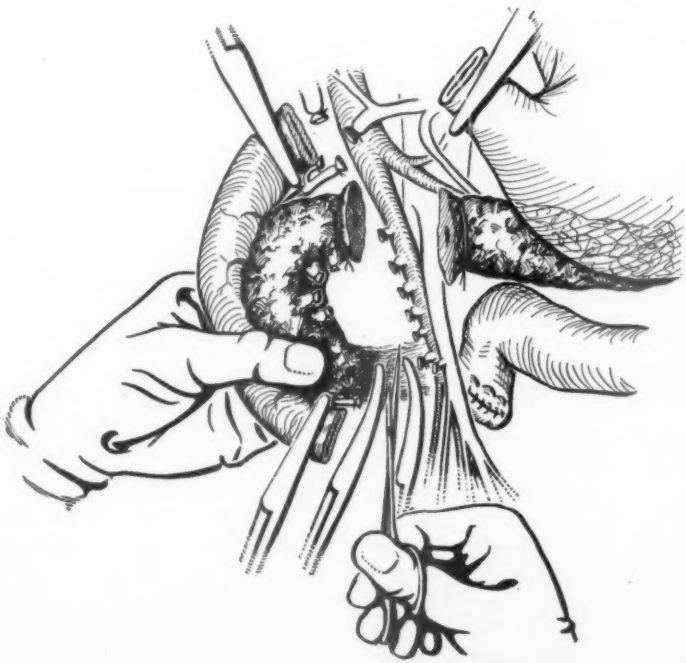

FIG. VIII. Liberation of uncinate process.

of dealing with these vessels than by clamping them with Cushing's clips or with artery forceps and attempting to tie them after division. If one of these veins is accidently torn during the dissection, a brisk haemorrhage results from what is virtually a hole in the side of the superior mesenteric or portal veins. It is then necessary to place a lateral ligature on the large vein which has been damaged. Case 4 died as a result of haemorrhage when one of these lateral ligatures slipped during the night following operation.

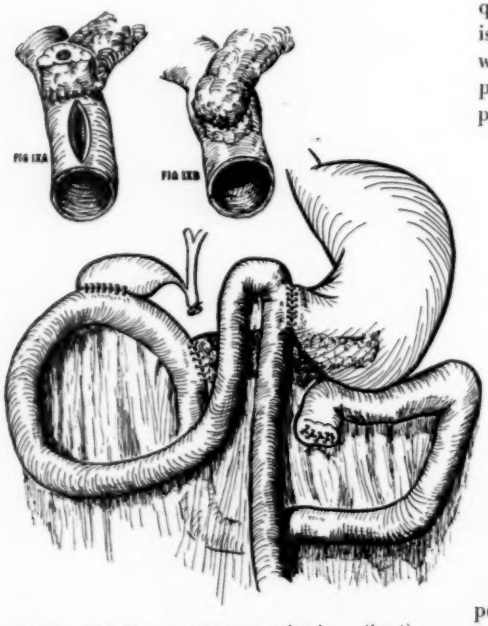

FIG. IX. The anastomoses showing (inset) how the pancreas is inserted into the jejunum.

The methods by which the uncinate process can best be freed is to pass the first two fingers of the left hand behind the pancreatico-duodenal mass, so that the latter lies in the palm of the hand, while the left thumb, flexing onto the two fingers behind, has the tip of the uncinate process well defined for clamping and cutting between Spencer Well forceps, just as one does in performing a thyroidectomy (Fig. VIII).

Having removed the pancreatico-duodenal segment it remains to anastomose the stomach and pancreas to the jejunum. Invariably we have joined the stomach and jejunum below the other anastomoses. This virtually leaves the proximal jejunum as a defunctioned loop into which the gall bladder and pancreas empty their contents. This may diminish the risk of cholangitis which frequently occurs when part of the biliary tract is anastomosed to a portion of the intestine which is actually transmitting food and the products of digestion. The stump of the pancreas is then implanted into a hole made in the side of the jejunum above the gall bladder anastomosis and held therein by a single row of silk sutures (Fig. IX).

RESULTS

The results of eight cases of pancreatico-duodenal resection are shown in Table 1.

These results indicate that the two post-operative deaths were due to technical errors which can be avoided. In the light of experience, the operation of pancreatico-duodenal resection should now be followed by a low mortality rate. The operation, as described, appears to be adequate in dealing with ampullary growths. It is less satisfactory for carcinoma of the pancreas as there is usually a greater extension of the tumour before the operation.

Earlier diagnosis should be the ambition of both physician and surgeon. When coupled with diligent surgery, far better results will be achieved.

TABLE 1

Case Number	Date of Operation	Site of Carcinoma	Stages	Result	Cause and time of death.
1	12/10/46	Ampulla	2	Alive and well March, 1952	——
2	17/11/45	Head of Pancreas	2	Died	Metastases after five months.
3	12/8/48	Head of Pancreas	2	Died	Metastases after nineteen months.
4	24/1/49	Head of Pancreas	1	Died	Haemorrhage from portal vein after twelve hours
5	8/5/49	Ampulla	1	Died	Ligation of hepatic artery. Died on second day.
6	1/9/49	Head of Pancreas	2	Died	Metastases after thirteen months.
7	12/4/50	Ampulla	2	Died	Metastases after twenty-one months
8	3/9/50	Ampulla	1	Alive and well March, 1952	——

SUMMARY

1. Early and accurate diagnosis of carcinoma of the pancreas and the ampulla of Vater can be assised by the use of biochemical tests and perhaps liver biopsy. Early laparotomy is essential to avoid further liver damage and spread of the tumour.
2. The general clinical improvement of the patients and the improvement of these tests have shown the value of preliminary decompression of the biliary system before pancreatico-duodenal resection. A two stage operation is therefore recommended.
3. The diagnosis of small tumours of the ampulla or head of the pancreas is discussed and its importance emphasised as the most difficult tumours to diagnose will probably have the best prognoses.
4. A detailed description of the steps in pancreatico-duodenal resection is given, with illustrations. The hazards are emphasized.
5. The results of resection in eight cases are recorded.

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MALIGNANT MELANOMATA

SOME POINTS IN TREATMENT AND PROGNOSIS

By J. Maxwell Clarke

Auckland

THE treatment of malignant melanomata will be considered under the following headings:—

(1) Prophylactic.

(2) Doubtful cases.

(3) When malignancy is certain.

Prophylactic treatment.

It is, of course, impossible to advise the excision of all pigmented moles or naevi, but it is of importance to keep in mind some guiding principles. Light brown moles may be left alone unless for cosmetic reasons, and it is generally believed that the hairy raised black patch rarely becomes malignant. The moles to be feared are the dark brown, black or blue-black ones which are subject to trauma or irritation. If, on a routine examination, one finds such a mole, then it is wise to advise its removal. It should be excised with a clear margin of healthy skin, and should always be sent to the pathologist for microscopic examination. No treatment should be applied to such naevi except complete excision. Diathermy, cautery, carbon dioxide snow should not be applied to the naevus or mole. There are cases in the Auckland Cancer Consultation series where malignant changes appear to have sprung into activity after such treatment.

Sections should not be taken out of a mole or suspected melanoma for microscopy unless the case is exceptional, as, for example, in a finger or a toe where the alternative is amputation. When such a section is taken, a pathological report should be obtained urgently, so that there will be a minimum of delay in carrying out further operative treatment if necessary. In children, before puberty, in very large pigmented naevi requiring plastic surgery, it appears to be free of danger to do such in operation in stages, removing part of the naevus at a time. Malignant changes in naevi in children are rare, but not unknown. It is of interest that 37 per cent. of malignant melanoma attending at the Auckland Consultation Clinic had no history of a pre-existing mole.

Doubtful cases.

In lesions which increase in size but slowly over the years, one may be in doubt as to the presence of malignant changes. Such naevi usually are of a low grade of malignancy, but if there is real doubt, they may be excised as for a pigmented naevus, submitting the tissue for an urgent pathological report. If this report indicates that there are malignant changes, or that there is doubt, a radical excision should be carried out within 2-3 days.

When malignancy appears certain.

When a pigmented naevus or mole shows some change, such as change of colour, increase in size after prolonged period with no apparent growth, or bleeding, it has almost certainly become malignant. The subsequent microscopic examination usually supports this diagnosis. Occasionally it may not do so, but the lesion still should be considered to be malignant. In such cases I think the clinical diagnosis is likely to be more reliable than the microscopic.

The treatment of malignant melanoma may be considered under the two headings:—

(a) The local lesion.

(b) The regional lymphatic glands.

(a) *The local lesion.*

There should be wide excision of a local lesion, removing skin normal in appearance wide of the microscopic lesion, aiming at a clear margin of two inches from the margin of the lesion. The deep fascia should also be removed. There should be a minimum of handling of the tumour. The

cutting diathermy may be used instead of the scalpel. In the face it may not be possible to keep so wide a margin in certain sites such as the cheek, nose and eyelids, but the excision must be radical, and, if necessary, we should call in our colleagues, the plastic surgeons, in such cases. The difficulty must not be side-stepped by doing a meagre excision. When the site is on a finger or a toe, amputation is indicated. In the female genitalia and in the anal region, radical excision is required when the disease is in an operable stage.

(b) *The regional lymph glands.*

The accepted practice at present is to perform a radical excision of the appropriate glands and gland bearing tissues within about six weeks of the excision of the primary lesion, whether the glands are clinically enlarged or not. There is no difficulty in carrying out this policy where the lesion is on a limb, but when it is situated on the trunk or on the midline of the head or neck, this policy may be impracticable.

The other course possible is to deal radically with the primary lesion and keep the patient under close observation, excising the glands if they become clinically enlarged.

I have not been able to find statistics in the literature which supported either view, so I shall now present some figures from the Auckland Consultation Clinic of the British Empire Cancer Campaign Society. The cases considered attended the Clinic between the years 1929-1946 inclusive. In a number of cases, who had initial treatment before attending the Clinic, the information was inadequate as to the early treatment. Some of these were in an advanced state when first seen at the Clinic. Some died after a short interval from other diseases. Some did not reply to follow-up notes. All such cases are excluded, and also all children under 14 years. Ninety cases remain for consideration (Table 1).

TABLE 1

RESULT OF TREATMENT IN NINETY CASES OF MALIGNANT MELANOMA AT AUCKLAND CONSULTATION CLINIC.

Type of treatment	No. of cases	Lived		
		5 years or over		Under 5 years
		Number	Percentage	
1. Local excision only of melanoma ..	37	17	46	20
2. Local excision plus excision of regional glands early. In 3 cases glands were positive microscopically. One case has lived 11 years	23	9	39	14
3. Local excision plus delayed excision of regional glands, i.e., 3 months after or longer. All glands microscopically positive	30	12	40	18
4. Group 1 and 3 combined. For delayed excision of glands means in most cases that local excision only has failed ..	67	29	43·3	38

These figures suggest that there is no advantage in the early excision of glands as a routine. The suggestion is that it is preferable to perform local excision and watch the patient for any enlargement of glands that may develop, but the difference between the two methods of treatment is so slight that it is not significant.

Further consideration of the "delayed excision" group is given in the following table.

TABLE 2

DELAYED GLAND EXCISION.

30 Cases.

Time interval between excision of primary lesion and excision of glands	No. of cases	Lived 5 yrs. or over
3 months to 6 months	8	Nil
6 months to 1 year	2	Nil
1–2 years	6	4
2–3 years	8	3
3–4 years	1	Nil
4–5 years	Nil	Nil
5–6 years	4	4
7 years	1	1

It is to be noted that in 10 cases where enlargement of glands occurred and excision was performed, between three and twelve months after excision of the primary lesion, there was not one case surviving five years after. This fact suggests that when the glands become enlarged within that period, the growth is very malignant, or conversely, that the resistance of the patient is low.

Other points of interest in regard to these ten cases are as follows:—

(a) *Sites.* Leg. 5 cases. Back, 2 cases. Toe, 1 case. Ear, 1 case. Thigh, 1 case. (See Table 3.)

(b) *Interval between probable onset of malignancy and excision of primary lesion.*

3 months or less. 5 cases
3 - 6 months. Nil.
6 - 12 months. 2 cases
1 - 2 years. 1 case.
over 2 years. 1 case (see Table 6.)
unknown. 1 case.

(c) *Size of primary lesion in cm.*

1 cm. 2 cases.
1.5 to 6 cm. 4 cases. (see Table 7.)
unknown 4 cases.

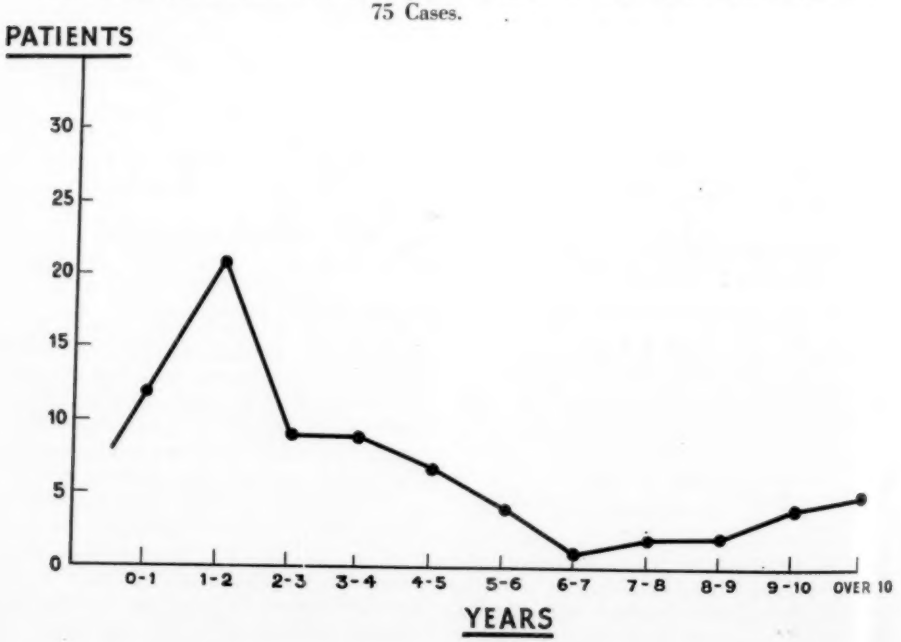
Graphs 1 and 2 show some points in regard to the mortality.

In Graph 1 the high mortality rate in the first years after treatment is shown.

GRAPH 1

NUMBERS WHO DIED IN SUCCESSIVE YEARS AFTER FIRST TREATMENT.

75 Cases.

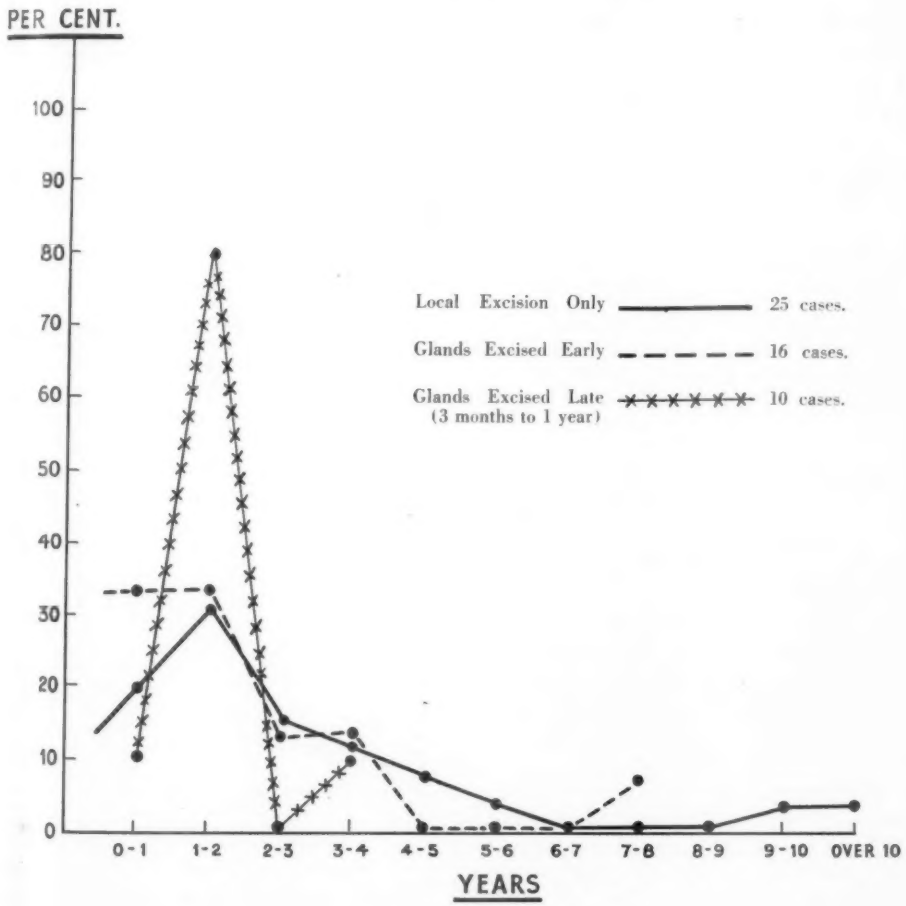


In Graph 2 the main point of interest is the curve showing the mortality in 10 cases whose glands were excised between 3 and 12 months after excision of the primary lesion. (Table 2.)

GRAPH 2

MORTALITY PERCENTAGES IN SUCCESSIVE YEARS WITH DIFFERENT METHODS OF TREATMENT

51 Cases



In Tables 3-7 other aspects of prognosis are considered.

TABLE 3

FIVE YEAR SURVIVALS ACCORDING TO SITE OF PRIMARY LESION

89 Cases Considered

Site	Total number	Surviving 5 yrs. or more		
		Number	Percentage	
Scalp	4	3	75	Head. 15 cases. 10 survived 5 yrs. or over. 66·6 per cent.
Face	6	3	50	
Ear	2	1	50	
Eyelids ..	3	3	100	
Neck	7	2	28·5	
Trunk ..	18	5	27·7	
Arm	6	2	33·3	
Thigh ..	12	3	25	
Knee region ..	3	1	33·3	Leg and foot. 25 cases. 12 survived 5 yrs. or over. 48 per cent.
Leg	18	10	55·5	
Ankle ..	3	0	Nil	
Foot	1	1	100	
Toe	4	2	50	
Finger ..	2	2	100	

The thigh, trunk and neck lesions appear to have the worst prognosis, while lesions of the head area, the leg, and the digits appear to be more benign.

TABLE 4

PROGNOSIS ACCORDING TO SEX IN 5 YEAR SURVIVORS

90 cases considered, sexes equal. 40 survivors.

Total — 40

Men — 13 — 32.5 per cent.

Women — 27 — 67.5 per cent.

The finding that there is a better prognosis in females is an unexpected one.

TABLE 5

PROGNOSIS ACCORDING TO AGE IN 5 YEAR SURVIVORS

Age	Total	5 yr. survivors	Percentage
Under 20	7	5	71
20–29 ..	11	6	54·5
30–39 ..	25	12	48
40–49 ..	15	7	46·6
50–59 ..	18	4	22·2
60–69 ..	10	4	40
70–79 ..	4	Nil	Nil
80 and over	Nil	—	—

The better prognosis in the younger age groups—under 30, is of some interest.

TABLE 6

Table showing relation between estimated duration of malignant change before excision and survival after excision. 54 cases considered.

Duration of lesion in years before excision	No. of cases	Survived 5 yrs. or longer	
		Number	Percentage
0–6 months ..	17	5	29·4
6 months – 1 year	12	5	42
1 year – 2 years ..	13	9	69·3
Over 2 years ..	12	8	66·6

In presenting this aspect of the problem, many of the clinic cases could not be considered as sufficient information was not available. In others, although the information was available, one could not estimate when a malignant change had supervened. In general, however, it would seem that the shorter the history, the greater the malignancy and the worse is the prognosis.

TABLE 7

PROGNOSIS RELATED TO SIZE OF PRIMARY LESION MALIGNANT MELANOMA

51 Cases.

Size of lesion in cm.	Survived.		
	5 years or over		Under 5 years
	Number	Percentage	
0 –1 ..	8	66·6	4
1·1–1·5 ..	3	50	3
1·6–2·0 ..	4	33.3	8
2·1–3·0 ..	4	44·4	5
3·1–4·0 ..	4	50	4
4·0 plus ..	1	25	3

Summary.

0 —1 cm. 66.6 per cent. survived 5 years or over.

1.1 — 3.0 cm. 41.0 per cent. survived 5 years or over.

3.1 cm. 42.0 per cent. survived 5 years or over.

From this Table it would appear that a small lesion 1 cm. or under, has a considerably better prognosis than a larger lesion.

SUMMARY

1. In a clinical study of 90 cases of malignant melanoma registered at the Auckland Consultation Clinic between 1929 and 1946, the evidence is slightly in favour of local excision only for the primary lesion with delayed operation on regional glands as required.
2. The prognosis in this series is considerably better in women than in men.
3. It is better in the younger age group.
4. Lesions in the head area, in the digits and in the leg appear to carry a better prognosis.
5. It would seem that the shorter the period between apparent onset of malignancy and operation, the worse is the prognosis.
6. With a small lesion, 1 cm. or less, there appears to be a better prognosis than with a larger lesion.

BENIGN NON-TRAUMATIC STRICTURES OF THE BILE DUCTS

By W. E. A. Hughes-Jones

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BENIGN non-traumatic strictures of the bile ducts are not common in the experience of any one surgeon who might be confronted unexpectedly with the problems incidental to such. The writer can speak only of 4 cases and these are in themselves representative of the lesions encountered, these being fibrosis of the ampulla, chronic obliterative cholangitis, diffuse or localized, and loss of the duct from neighbouring inflammation. As illustrating the relative frequency of these conditions, Cattell (1947) found that in 123 instances of benign stricture of the bile ducts 99 were due to operative injury, 11 to cholangitis and 9 to fibrosis of the ampulla. Amongst 54 such patients Carter *et alii* (1950) speaks of 12 cases of chronic obliterative cholangitis (4 intrahepatic and 8 of the common hepatic duct), 6 cases of fibrosis of the ampulla and 1 of fibrosis of the common duct due to ulceration by a stone.

In some instances of benign stricture the common duct has been opened at a former operation and the doubt arises whether this is not really another example of traumatic stricture but it is useful to recall Cattell's (1947) observation that at the Lahey Clinic not one stricture had followed the exploration of the common bile duct in 1800 patients. Speaking of this doubt, Carter *et alii* (1950) think there are no clear distinguishing features between fibrosis associated with trauma (excluding admitted injury of the duct) and that due solely to inflammation.

Infection within the obstructed duct is usual. Carter *et alii* had positive cultures in 24 of 38 patients in whom bile cultures were made, 20 being *Bacillus Coli*, one *Bacillus Coli* and *Bacillus Welchii*, and 3 Haemolytic streptococci. In 21 patients with pre-operative chills and fever 18 had positive cultures. Incidentally, he commented without offering evidence that antibiotics appeared to play little or no part in eliminating organisms from the biliary tract.

Fibrosis of the Ampulla

While this name should be retained it must be understood to include a condition other than fibrosis, that is, a relative and equally intractible narrowing of the ampulla in the presence of great permanent dilatation of the common duct. Cattell (1947) thought that insufficient attention had been called to this form of benign obstruction, that it was probably much more frequent than realized and frequently unrecognized and that it was usually found in patients with recurrent calculi in the common duct.

Mrs. O. R., 71 years, suffered from biliary colic in the later months of 1946. In January, 1947, following pain, fever and jaundice for ten days, at operation the gall bladder containing a large calculus and much small calcareous debris was removed and the dilated common duct explored, much pultaceous biliary mud being evacuated and duct forceps being passed into the duodenum, the ampulla being stretched with the forceps.

In April, 1947, hepatic intermittent fever began to recur each month and there was much loss of weight. In July, 1948, a second operation disclosed gross adhesions, a thick-walled common duct more than ¾" across, clear yellow bile, and a mass of biliary mud and debris 1½" x ¾" in the lowest part of the duct. After removal of the debris an unsuccessful search for the ampulla was made. The common duct was drained.

Convalescence was marred by a probable extension of an intra-cranial aneurysm and difficulty in maintaining fluid balance, only resolved by closure of the biliary fistula.

In February, 1950, colic with fever and rigor was again occurring each week, without obvious jaundice and without liver enlargement. In March, 1950, at a third operation the grossly thickened distended common duct was emptied of a great mass of biliary mud, stones and debris, this mass extending for over 4" upwards. The common duct was divided and anastomosed to a free end of jejunum prepared en-Y.

To the time of writing, there has been a steady increase in weight, no further biliary pain, and improvement in health as far as is allowed by the troublesome intra-cranial pain and ophthalmoplegia.

With a fuller understanding at the time of the second operation of the problem of relative stenosis of the ampulla adequate drainage of the common duct should have been made and so a third operation avoided.

DIFFUSE CHRONIC OBLITERATIVE CHOLANGITIS

Cole (1948) observed several centimetres of fairly normal common duct at one operation but at an operation several months later found that portion of the duct to have stenosed down to a structure with a lumen scarcely as large as a fine probe. He commented that suppurative cholangitis rarely gives rise to stricture formation. Cattell (1947) speaks of a long-standing inflammation of the common hepatic or common bile duct with in some a fibrotic narrowing of the entire extra-hepatic ducts. Earlier (1943), he noted the infrequency of this stenosis apart from gall-bladder disease and thought that inflammation of the ducts was most apt to occur in neglected gall-bladder disease. In that earlier paper he commented that the end-result of recurrent cholangitis may be a fibrous duct with a greatly diminished lumen.

Mrs. J. first suffered from biliary colic in 1928 but, when aged 61 years in September, 1946, the attacks recurred frequently. Her general health was not good but she demanded relief from pain.

In July, 1947, at operation, the gall-bladder was removed, the distended common duct emptied of biliary mud and the ampulla stretched gently, during which there was troublesome bleeding but no question of any gross damage of the ducts. She was very ill from pneumonia, recovering slowly.

In July, 1948, she reported that ever since operation she had suffered each month from fever, severe chills and jaundice, recovering well between attacks, and was found to have a large, tender liver. At the second operation in August, 1948, the common duct, lying behind the right lateral border of the portal vein, was found dilated above at the *porta hepatis* containing debris of mud without stones and an old suture and grossly narrowed and thickened below so that graduated sounds were passed only with difficulty. The duct was drained.

In April, 1949, frequent hepatic intermittent fever returned and in November, 1949, the liver was enlarged and tender. In that month at the third operation, the common duct and common hepatic duct were found very thickened and sclerosed with almost no lumen. As the incision in the duct was extended upwards following the minute lumen, no bile resulting meanwhile, a point was suddenly reached near the *porta hepatis* at which an appreciable, but not dilated, lumen was entered and biliary debris, many very small stones and much bile flowed out with force. This part of the duct was surrounded at the *porta hepatis* by the free end of a defunctioned section of jejunum prepared en-Y.

In June, 1951, she was well, had gained much weight and the liver was not enlarged. At the time of writing the hepatic intermittent fever has returned and there is without doubt further stenosis.

What part the undoubted difficulty at the first operation, due both to bleeding and to the anatomical peculiarity of the position of the duct behind the portal vein, played in the development of the stenosis of the duct is a matter for speculation, but it is certain that there was no gross damage of the duct at the first operation. The extensive stenosis of the duct with thickening of the wall and hyperaemia of the scanty mucosa was strongly suggestive of diffuse chronic obliterative cholangitis.

LOCALIZED CHRONIC OBLITERATIVE CHOLANGITIS

Cattell (1943) noted that inflammation with fibrosis may involve limited portions of the intra-hepatic ducts forming a small area of stricture which is only discovered by probing.

Mrs. E.B., 62 years, in December, 1946, developed continuous jaundice, varying in intensity, with loss of weight and hepatic enlargement. In March, 1947, at operation, a large, hard, white mass at the site of the gall-bladder, and an impassable obstruction in the upper part of the common hepatic duct, were thought to be malignant and a piece of the gall-bladder mass was taken for section. The histological report was that in a general groundwork of fibrous tissue there was a diffuse permeation with small round cells, plasma cells and a few polymorph leucocytes. In April, 1947, at a second operation, all the former appearance and consistency of malignancy had vanished leaving an intensely thickened gall-bladder. After removal of the gall-bladder its wall was seen to be $\frac{1}{2}$" thick containing no mucosa, it contained a number of facetted stones and most offensive pus. The mass at the *porta hepatis* had disappeared and the common duct was not explored.

In July, 1948, sharp pain was followed by jaundice without chills. At the third operation in August, 1948, the liver had the appearance of

obstruction, the common duct contained no stones and duct forceps were passed easily into the duodenum, but passage of the forceps up the duct was stopped by a hard mass within the *porta hepatis* and in the liver. A thin probe was all that could be passed through a stricture and this was followed by a considerable rush of clear, dark bile with no calculous debris. The stricture was dilated gradually, was up to ½" long, and through it was passed a metal tube anchored by linen thread. Histological section of the stricture showed fibrous tissue along one edge of which were remnants of simple columnar epithelium beneath which were numerous inflammatory cells mainly small round cells.

In January, 1951, there was loss of appetite and weight and in May, 1951, great wasting, deep jaundice and severe pain, without liver enlargement but with tenderness. In that month at the fourth operation the metal tube full of calculous debris was 1¼" lower in the duct. After various manoeuvres two small openings were found in the grossly narrowed upper end of the hepatic duct and were dilated with graduated sounds, very little bile and debris flowing. A vitallium Y-tube was fixed in position with a wire suture. After operation there was copious drainage of bile.

At the time of writing she is reported well but the danger of blockage of the tube and of further fibrosis are not under-estimated.

This case illustrates the problems and hazards of obliterative cholangitis and emphasizes the unfortunate need for multiple operations.

Loss of the Duct from Neighbouring Inflammation

Cole (1948) pointed out that severe neighbouring inflammation could cause stenosis of the duct, having found this on three occasions in association with pylephlebitis and at other times with a small abscess or small collection of bile. In the case here reported the evidence pointed to loss of the duct by sloughing as a consequence of suppuration.

Mrs. G.L., 29 years, began to suffer from persistent vomiting after meals in the middle of 1949 and in the latter part of that year cholecystectomy was done after radiological investigation but no convincing disease of the gall-bladder existed. The operation was done by a careful, good surgeon who met with no difficulty during the operation and who was satisfied that the common duct was normal at the end of the operation, proceeding then to removal of the appendix. After two days fever was followed by copious drainage of pus and bile. The biliary fistula closed after two months with the onset of jaundice. The surgeon then performed a second operation, found that the lower supraduodenal portion of the common duct was completely missing and anastomosed the long proximal portion to the duodenum over a T-tube.

In December, 1950, jaundice recurred and persisted in varying degree, with a little hepatic enlargement.

In May, 1951, at the third operation, the duct was found completely isolated from the duodenum and with no communication with the intestine. Again the proximal part of the duct was comparatively long and ended in such a cap of very thickened wall that when it was freely incised and opened the end of the duct immediately closed. Fearing that stenosis would follow any unsupported anastomosis to the intestine a vitallium tube was sutured into the end of the duct and an anastomosis made to the jejunum prepared en-Y.

At the time of writing she remains well.

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SCLEROSING PERI-ANGEITIS OF THE LATERAL THORACIC WALL

By E. S. R. Hughes

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THE lesion about to be described is unusual; it is characterized by the appearance of an indurated and usually sensitive "cord" in the dermis and subcutaneous tissue of the thoracic and upper abdominal wall. This "cord" is 2 to 3 mm. thick; it may be single or accompanied by one or more parallel and similar structures. The "cord" or "cords" are situated just medial to the anterior axillary line, and, beginning near the level of the umbilicus, extend directly upwards to cross the sub-costal margin. In some cases the "cord" appears to end lateral to the nipple at the lower border of the *pectoralis major;* in the remainder it crosses the sub-mammary sulcus and ends in the lower and outer quadrant of the breast. In these latter cases it may be traced to the nipple, retaining throughout its dermal position. The overlying skin may be elevated into a thin ridge, or actually retracted into a groove. In none of my cases was there any discolouration of the overlying skin.

The appearance of the "cord" is usually preceded by a mild ache. It gradually disappears over a period of several weeks. It is rarely bilateral, and apart from an apparent relationship to abnormalities of the breast, it has no important significance (Table 1).

TABLE 1

Certain clinical features of 39 cases recorded in the literature, including the 5 recorded here.

Sex:	Males 14. Females 25.
Side:	Right 16. Left 16. (7 unknown)
Age:	20 years to 55 years.
Associated findings:	9 cases had fibroadenomas of the breast.

Clinical Review

In 1922, Fiessinger and Mathieu described 3 adult patients, 2 females and one male, in each of whom was a smooth, hard cord beginning at about the level of the umbilicus and ascending vertically upwards across the costal margin towards the right breast.

Williams (1931) reported a man of 40 years who, ten days previously, became aware of a tender cord-like structure under the skin just lateral to the right anterior axillary line, which began below the costal margin and disappeared under the inferior border of the *pectoralis major.*

In the following year Daniels (1932) described 5 further cases. In 3 of these a tender cord coursed upwards to a point just lateral to the right nipple; in a fourth patient the rounded cord passed close to the left breast, and in the fifth, a male of 50 years, a tender cord-like structure extended from the fourth to the seventh interspace, on the right side. Daniels, and the earlier authors, believed the condition to be a "thrombo-phlebitis."

In 1933, Moschowitz discussed a series of patients with similar clinical features. In a female of 39 years he noted a groove extending between the left breast and axilla, whilst below and beginning at the lower margin of the breast, and extending distally, there was a cord which felt similar to a *vas deferens.* In a second female, a vertical cord could be traced for about eight inches, in the nipple line, and in a third case, a cord which felt like a *vas deferens* could be palpated on the anterior wall of the axilla, while strands were also present below the breast. Moschowitz suggested that the lesion be termed "Vestigial Mastitis."

Robinson (1935) reported 2 cases, in both of whom a string-like structure under the skin extended upwards from the costal margin just behind the breast, and disappeared under the anterior axillary fold. Robinson regards the condition as an "effort" thrombosis (personal communication).

Le Lorier (1937) described a woman of 23 in whom a cord extended distally from the left axillary region. In the mammary part of this cord the skin was adherent and, on displacing it, the phenomenon of *peau d'orange* appeared. At its two extremities it disappeared into the surrounding tissues.

Mondor (1939) recorded 4 similar cases. The cord descended from the breast to the lower costal margin and on palpation felt like a ureteric catheter. It was partly adherent to the skin and, in one case, he observed the overlying skin to be puckered above and raised below, whilst 1 cm. behind there was a more filiform but similar structure.

Nylander (1941) reported a female of 34 years in whom was observed a cord 2 mm. thick which began 1 cm. below the areola of the nipple and extended distally for 8 cm. Above it seemed fixed to the skin and not clearly distinguished. In a man of 43 years a cord as thick as a thin lead pencil began above, close to the breast and crossing the costal arch, ended midway between the costal margin and anterior superior iliac spine. He referred to similar findings in 3 other female patients.

In 1944, Mondor described 3 more cases; in one a hard, tender cord extended from the sub-mammary fold to the iliac spine; in another, a cord as thick as a knitting needle extended from the breast to the costal margin, and seemed adherent to the deep surface of the skin. Calvet (1944) and Leger (1947) recorded further cases.

Delannoy, Driessens and Verhaeghe (1947) described 2 cases in which the lesion extended from the sub-mammary sulcus to the edge of the costal margin; the cord presented a beaded appearance, and a similar structure ran parallel with it. In Mazingarbe's case (1947), three cords could be seen passing distally from the sub-mammary fold. Perrin (1947) reported two cases and emphasised the intra-dermal position of the cord. Sicard (quoted by Perrin [1947]) recorded a typical case wherein the cord began in the sub-mammary fold at the junction of the middle and outer thirds and descended vertically; it appeared fixed in the skin. Diamant-Berger (1949) noted a case with three parallel cords on the abdominal wall but could not trace them above the costal margin.

FIG. I. Case 1. Mrs. I.S. The left breast has been lifted to reveal the lesion.

CASE REPORTS

Case 1.

Mrs. I.S., aged 40 years, a housewife, had noticed a lump, "the size of a cherry," in the upper half of her left breast nine weeks previously; within a fortnight it had disappeared. A few days later

she became conscious of an ache in the left side of her chest and then discovered a long ridge under the breast. On lifting the breast three or four parallel ridges could be seen extending vertically downwards from the lower and outer quadrant to just beyond the costal margin. The ridges were caused by cord-like structures apparently within the dermis itself. For a short distance the skin overlying one of the cords was retracted into a groove (Fig. I).

FIG. II. Photomicrograph (low power) of a section from Case 1 showing the dermis and the underlying subcutaneous tissue. In the subcutaneous fat there is a small ovoid nodule in which there are two well-defined structures each containing a lumen and with a ring of tissue a short distance from the lumen. The general resemblance to two small vessels with some peri-vascular fibrous thickening is unmistakable. (x 20.)

A biopsy examination was done. On histological examination the section is a piece of skin and subcutaneous tissue cut at right angles to the cord of tissue which was observed clinically (Fig. II). The dermis is normal and is well defined from the deeper subcutaneous tissue. In the subcutaneous tissue there is a somewhat irregular ovoid mass composed of spindle cells and some collagenous tissue. Most of the cells are fibroblasts but there are a few smooth muscle cells amongst these.

In this mass there are two endothelium-lined spaces around which the spindle cells are arranged concentrically; there is a thin ring about two cells thick which is about six cell-layers away from the lumen. This ring of tissue is composed of smooth muscle. Amongst these spindle cells there are a few wandering cells mainly of the small round cell type but an occasional polymorphonuclear leucocyte may be observed (Figs. III and IV).

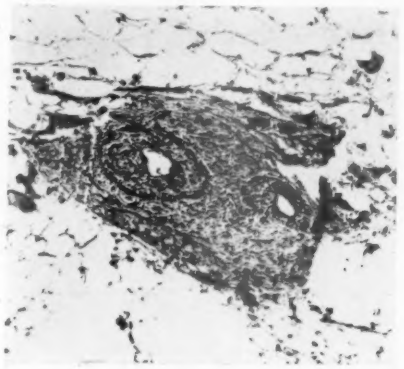

FIG. III. Photomicrograph of the small nodule seen in the subcutaneous fat in Fig. II. The structures resembling vessels are well seen and the surrounding spindle celled tissue is clearly defined from the surrounding fat. (x 75.)

The two endothelium-lined spaces appear quite definitely to be vessels, with the original form of the muscle wall being indicated by the ring of muscle tissue. It is clear that there has been an increase in connective tissue internal to this line but the predominant lesion is a gross proliferation of tissue outside it.

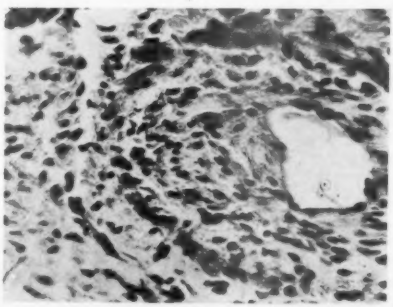

FIG. IV. Photomicrograph (high power) of portion of the wall of one of the spaces seen in Fig. III showing the endothelium lining the space, the general spindle cell form of the tissue and a few wandering cells scattered through this. (x 350.)

It is not possible to say whether the vessel was artery, vein or lymphatic, though the presence of an occasional erythrocyte in the lumen suggests that the structures are blood-vascular rather than lymph-vascular in type.

Case 2.

S.G., a male patient, aged 45 years, developed a mild ache in the right side of his chest three weeks previously; a week later he noticed a cord-like structure in the skin on the right side of the chest which gradually became more and more apparent. Examination showed a ridge of skin extending vertically downwards from the level of, but 5 cm. lateral to, the nipple; it was single at first but soon bifurcated and the two branches extended downwards together, separated by 1 to 2 cm., almost to the costal margin. At the level of the sixth rib, the overlying skin was retracted into a groove. The ridge seemed to be caused by fine indurated cords, 1 to 2 mm. thick and situated apparently within the dermis. Just medial to the nipple line there was a supernumerary nipple (Fig. V).

FIG. V. Case 2. Mr. S.G. The lesion can be seen crossing the sixth, seventh and eighth ribs on the right side.

A biopsy examination was done. On histological examination it is clear that the specimen here is cut at right angles to the clinically observed cord of tissue.

The dermis is normal and is clearly defined from the subjacent connective tissue; projecting from the deeper layer of the dermis there is a rounded mass of cellular tissue in which there are two lumina. These are lined by endothelium-like cells.

The nodule is composed of spindle cells with certain amount of collagenous tissue. Most of these cells are fibroblasts but there is an occasional smooth muscle cell.

In addition to the main lumina described there are also small capillary spaces scattered through the nodule (Figs. VI and VII).

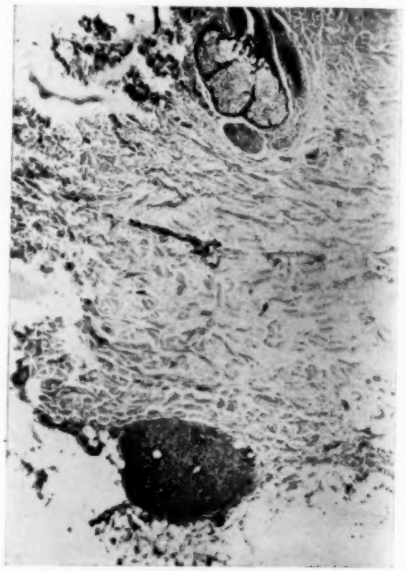

FIG. VI. Photomicrograph (low power) of a section from Case 2. Projecting from the deeper layer of the dermis is a rounded mass of cellular tissue in which there are two lumina. (x 25.)

The two main lumina are interpreted as vascular spaces which are the remnants of originally small vessels. Whether these are the lumina of main vessels, surviving and somewhat prominent *vasa vasorum*, or some new formed and somewhat dilated capillaries developing in an organizing connective tissue is in the present state of our knowledge, not clear. When the macroscopic form of the lesion is taken into consideration with the histological appearances (quite apart from any similar examples) it is concluded that the lumina represent two original vessels. These vessels, of course, may have been very closely inter-related and perhaps communicating.

The essential feature is a tremendous increase in the amount of tissue in and around the vessels.

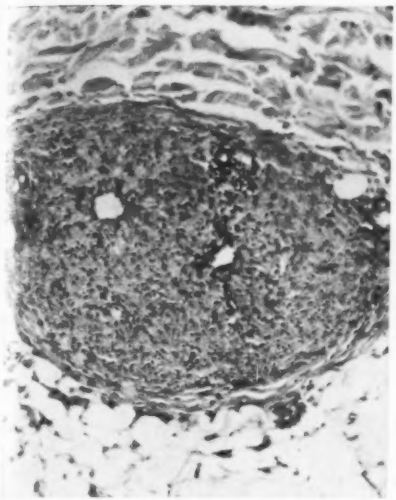

FIG. VII. Photomicrograph of the nodule seen projecting from the deeper layer of the dermis in Fig. VI. Two main lumina can be seen as well as small capillary spaces scattered through the nodule. (x 75.)

Case 3.

Mrs. A.G., aged 42, housewife, had suffered from pain in the left breast for some time. Examination revealed a localised area of chronic mastitis in the upper and outer quadrant of this breast. A wedge excision of the affected part of the breast was performed. The wound healed by first intention. Following operation, she developed an ache in the chest wall on the same side, together with a peculiar sensation in the nipple. Three weeks later she observed a cord-like structure under the left breast. Examination revealed two roughly parallel cords which extended from the nipple across the sub-mammary sulcus and vertically downwards to just below the costal margin. The overlying skin was retracted into a groove over portion of the inner cord; no biopsy was performed and the condition slowly subsided.

Case 4.

L.R., a male, aged 30 years, whilst undressing, observed the left side of his chest to be tender. On investigating he found this tenderness to be caused by, what he believed to be, a thrombosed vein to the outer side of the breast. Examination showed a cord 2 to 3 mm. thick which began at the lower border of *pectoralis major* at the level of the third rib and extended as far as the eighth rib in the anterior axillary line. The cord was in the dermis and for part of its course raised a ridge in the skin and for part caused its retraction into a groove. There was an accessory nipple below and medial to the nipple line (Fig. VIII).

A biopsy was done and on histological examination the general appearances of the section are similar to those seen in the preceding cases. The dermis is well defined from the subcutaneous tissue and in the latter there is a somewhat rounded nodule (in section).

FIG. VIII. Case 4. L.R. The lesion can be seen lateral to the nipple. The overlying skin is partly raised and partly retracted.

This is composed of spindle cells which are arranged concentrically around what appears to have been a lumen. This middle zone is almost completely replaced by some fibroblasts and many wandering cells, some of the polymorphonuclear leucocyte form. Around these is a thin layer of cells which, by the staining characters is smooth muscle.

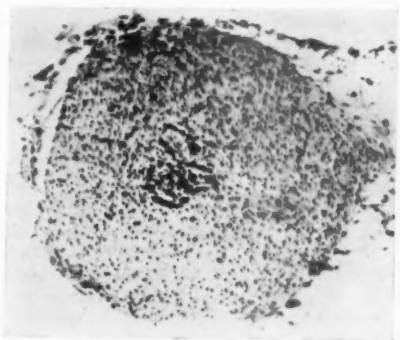

FIG. IX. Photomicrograph of a section from Case 4. The nodule is composed of spindle cells arranged concentrically around what appears to have been a lumen. The general form of the lesion is circular and is well defined from the surrounding tissue. (x 75.)

The principal part lies external to this muscle layer and is composed almost entirely of spindle cells. The general form of the lesion is circular and is well-defined from the surrounding tissue. Amongst the cells of this part are numerous small capillaries (Figs. IX and X).

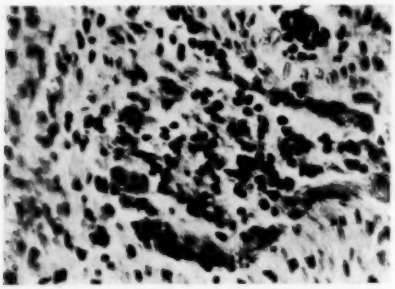

FIG. X. Photomicrograph (high power) to show the middle zone of the nodule seen in Fig. IX. This middle zone is almost completely replaced by some fibroblasts and many wandering cells, some of the polymorphonuclear leucocyte form. Around these is a thin layer of cells which, by the staining characters, is smooth muscle. (x 350.)

Here again in view of the macroscopic features, the structure is interpreted as being a vessel, the intima of which is so thickened and so infiltrated with wandering cells that the lumen has practically disappeared; the adventitia, also, has become grossly thickened and fibroblastic.

Case 5.

Mrs. V.W., aged 32, complained of a painful, cord-like thickening on the right chest wall which had first appeared three months before. At first the cord was only 5 cms. long but within three weeks had extended from the breast to upper abdomen. Examination revealed a cord apparently within the dermis, which began in the lower and outer quadrant of the breast and extended almost vertically downwards to disappear just above the level of the umbilicus. About 2 cm. below the breast the cord appeared to bifurcate and the two branches proceeded distally together. There was a chronic mastitis affecting both breasts.

A biopsy was performed and histological examination made. The dermis is normal and well demarcated from the underlying subcutaneous tissue. At one part on the deep aspect of the dermis there is a thickening which projects into the subjacent fat.

This is composed of numerous spindle cells and some collagenous material. Most of the cells are fibroblastic in form but there are a few scattered muscle cells.

FIG. XI. Case 5. Mrs. V.W. The "cord" can be seen passing down the chest wall; it has bifurcated and the two branches are easily seen for most of its course.

This differs from the ones previously described in that there is not such a clear indication of a lumen but there are a few endothelium-lined spaces, one of which is rather larger than the others; examination of these areas show that these spindle cells are orientated round this lumen in a way suggesting that it may have been the lumen of some pre-existing vessel. In this region, as in the last case, there are many wandering cells, both of the small round, and of the polymorphonuclear leucocyte type and these are more prominent and abundant than in other parts of the section.

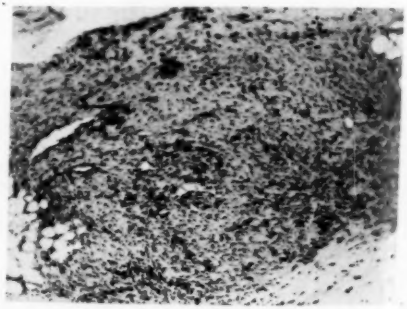

FIG. XII. Photomicrograph of a section from Case 5 to show one of the "cords" in section. There is not such a clear indication of a lumen as in the previous examples but there are a few endothelial-lined spaces, one of which is larger than the others. (x 75.)

The peripheral part of the nodule is composed of a cellular connective tissue which is somewhat more irregular than in the other cases and extends for short distances in various directions, particularly into the fat. This is interpreted as being an inflammation of a vessel with almost complete destruction and replacement of the vessel wall, with loss of the lumen by thickening of the adventitial tissues (Figs. XII and XIII).

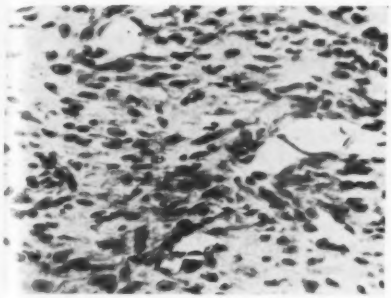

FIG. XIII. Photomicrograph (high power) to show the middle zone of the nodule seen in Fig. XII. There are many wandering cells, both of the small round, and of the polymorphonuclear leucocyte type; these are more prominent and abundant here than in other parts of the section. (x 350.)

DISCUSSION

In his first case Mondor (1939) described a vessel with endothelial proliferation, whose walls were composed of several thin elastic fibres. In a neighbouring section there was a nodule of bone which he considered was an area of metaplasia organized in a thrombus. After histological examination of this case he believed the condition to be one affecting the lymphatics rather than the veins, though his uncertainty is reflected in the term to describe it, that is, *tronculite sous-cutanée subaigue*. In his second case (1944) the altered vessel was situated near an artery; its walls were composed of an outer layer of matted connective tissue containing smooth muscle and an inner layer of swollen endothelial cells; this time he termed the lesion *phlébite en cordon* and this has been used by subsequent authors.

Nylander (1941) observed a thickened blood vessel deep in the subcutaneous tissue with well preserved endothelium, surrounded by connective tissue and muscle cells. There was no thrombus. In a second case there was a small blood vessel with thickened walls composed of fibrillar connective tissue, fibroblasts, and many lymphocytes. Mazingarbe (1947) found alteration in structure of certain of the vascular walls, with a tendency to obliterative sclerosis. He was unable to interpret the pathological changes and believed that no frank analogy existed between his case and that of Mondor. In Perrin's case (1947) a vein was obliterated by thickening of its inner coat; the walls were oedematous and composed of connective tissue and muscle fibres without elastic fibres. In some parts a lumen persisted and red blood cells could be seen within it.

Moschowitz (1933) found a totally different lesion, though his cases were clinically identical. He observed epithelial tubules, lined by flattened and columnar cells, lying within a connective tissue matrix, and surrounded in places by a considerable number of lymphocytes intermingled with occasional polymorphonuclear leucocytes and plasma cells.

Moschowitz believed that the epithelial portion of the mammary line persisted and that this lesion represented "a vestigial mastitis." His photomicrographs are not convincing, however, nor have his histological descriptions received any confirmation.

In addition to the cases specifically examined here, specimens obtained elsewhere have also been reviewed and, in all, nine cases have been investigated histologically. These occur in various forms which differ somewhat, but in general show certain common features:—

(1) One or more lumina (shown well in cases 1 and 2—Figs. II and VI).

(2) Thickening of the intima is at times almost complete, but some indication of the lumen can usually be found.

(3) Gross thickening of the adventitia which may occur in two forms:

  (a) Localized and giving the appearance of a grossly thickened vessel (Case 4—Fig. IX);

  (b) A more profuse and irregular lesion (Case 5—Fig. XII).

(4) Predominantly connective tissue proliferation with some smooth muscle tissue.

(5) The presence of wandering cells of both the small round and polymorphonuclear leucocyte type. The proportion of these varies from case to case.

When it comes to the interpretation of these appearances the problem is the same as in other conditions. There is a clear indication of spatial relationships at one

particular stage of the progress of the condition; but the problem is to interpret this in terms of time relationships, that is to say, in what direction are the processes proceeding and to what extent is the condition changing.

In this symptom complex it is known that the changes are fairly rapid because the life history of the condition is a matter of about ten to twelve weeks. Therefore, if these conditions be related, it should be possible to correlate the various examples in some way to indicate their mode of development.

The lesions can be graded according to their apparent histological age and if this is done then Case 1 should be the youngest lesion, Case 2 somewhat older, Case 4 older still and Case 5 should be the oldest of the series. This is found, in fact, to be so with the exception of Case 4. Whether the lesion here is different or the process more rapid, or there is some oversight on the part of the patient is not apparent.

Regarding the nature of the lesion there is no question but that it is an inflammatory one. There is no justification for the view that it might be neoplastic. The clinical history with disappearance of the lesion in about twelve weeks makes this clear. In addition the histological appearances are those of a sub-acute inflammatory condition.

The aetiology is not apparent, and indeed it is not even suggested by the histological appearances. It is extremely doubtful if it is traumatic in origin because:—

(a) There is no indication of haemorrhage (new or old) in these sections.

(b) Organization of damaged tissue gives a more diffuse and irregular lesion.

(c) As a corollary of this, the histological appearances of organizing "granulation tissue" would be seen arising from multiple foci, and not from the single line focus.

All that can be said is that the aetiology is uncertain and any further cases should be investigated bacteriologically (both for bacterium and virus) and it remains for the future to clarify the point.

Regarding terminology, although several names have been given, it seems that the essential features common to all cases have been overlooked. In the absence of more precise aetiological information the prominent morphological features have usually been accepted as providing the best nomenclature. The French suggestion of a lesion *en cordon* is a good one but provided that the name includes reference to vessels, it is not necessary to emphasise the fact that the clinical lesion is in the form of a cord. The important point is that there is gross sclerosis and that this is mainly round some vessel or vessels and therefore the name suggested here is "Sclerosing Peri-angeitis of the Lateral Thoracic Wall."

SUMMARY

An unusual lesion affecting the lateral chest wall is described; 5 cases are reported and the literature on the subject is reviewed. Histological examination indicates gross sclerosis around some vessel or vessels.

ACKNOWLEDGEMENTS

I am indebted to my colleagues for referring to me certain of the cases reported here.

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FACIAL NEURALGIAS

By R. A. Money

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THE subject of facial neuralgia always presents a difficult problem, but an endeavour will be made to clarify the diagnosis and treatment of some of the several varieties under the following headings:—

1. Trigeminal neuralgia (*tic doloureux*).
2. Trigeminal neuritis and post-herpetic neuralgia.
3. Anterior migrainous neuralgia.
4. Neuralgia of vascular origin.
5. Sympathetic hemi-crania.
6. Chronic neuralgia of the face and jaws. ("Atypical facial neuralgia.")
7. Costen's syndrome of temporo-mandibular joint strain.
8. Neuralgias due to cranial and extra-cranial tumours (including aneurysms).
9. Neuralgias of central origin.

Migraine and its manifestations will be omitted, as in these cases most of the pain is referred to the head and scalp; and the neuralgias of nasal and ocular origin will receive adequate consideration from other members of those specialities.

1. Trigeminal neuralgia.

Trigeminal neuralgia or *tic doloureux* is the commonest of the facial neuralgias; and, despite much high-level electronic neuronal research work, careful clinical observations and detailed pathological studies, its real causation remains unknown.

It occurs mostly in elderly and edentulous females and is at first limited to the distribution of one or more branches of the trigeminal nerve. It begins usually in the second or third divisions, rarely in the first division, although it may subsequently spread there.

The pain is very characteristic, and unless it conforms to certain definite features, the diagnosis should be questioned. First of all, it is paroxysmal, spasmodic, and of short duration and spontaneous remissions occur for weeks, months or years. The pain is described as stabbing, lancinating and excruciating. It may be induced by cold air currents, by light touch at one or more of the "trigger" points, by eating and drinking, and by washing the face, especially with cold water.

Each paroxysm is accompanied by an autonomic disturbance in the area of distribution of the pain, that is to say, flushing of the skin, salivation and, if the first division is involved, lachrymation.

Treatment

In the early stages and in the first few attacks, relief may be afforded by the giving of the well known Gower's mixture containing gelsemnium, chloral-butyl hydrate, and *liquor trinitrini, etcetera.* Large doses of Vitamin B.1. by intra-muscular or intravenous injection will frequently keep the severe pains in check for a time, and inhalations of Trilene at regular intervals will often help.

When the above measures have failed, injections of alcohol into the peripheral portions of the affected root are worthwhile, especially for supra-orbital and infra-orbital neuralgias; or else avulsions of these nerves, under local anaesthesia, may be performed.

In elderly poor-risk cases, alcohol injections of the third and second roots inside the skull, or even of the Gasserian ganglion itself, via the *foramen ovale,* will give worthwhile relief for months or years, or at times, permanently.

However, in persons in good general condition, it is wiser to advise a fractional or complete resection of the posterior sensory root of the Gasserian ganglion, in Meckel's cave. This is best performed, with the patient sitting upright in an adapted dental chair, and via the sub-temporal extra-dural route. By careful dissection in a dry field and with

a good light, sufficient ophthalmic division fibres to nourish the cornea and the motor root, can be spared. Care must be taken not to drag on or avulse the greater superficial petrosal nerve, as this may result in facial palsy.

More recently, some neurosurgeons have been performing this operation via an intra-dural sub-temporal approach, which is said to give easier access to the posterior root with less risk of haemorrhage from the middle meningeal artery, or of producing facial palsy.

Where the pains involve the ophthalmic division, Dandy's unilateral sub-occipital approach, with division of the sensory root close to the pons, is preferred, as, when sectioned at this level, its trophic function in relation to the cornea, seems less likely to be disturbed. When exposed in this approach, the fifth nerve is often found stretched over an aberrant artery, which Dandy has claimed may be the cause of the pain.

Despite the safety and the low mortality rate of the skilfully performed sub-temporal operation, many patients still prefer to have, and ask for, alcohol injections. Although they are usually only temporary in effect, and the adhesions they produce in the nerves and in Meckel's cave make subsequent operations more difficult, yet, if successful, they give the patient a period of rest and respite, and indicate the degree of numbness and wooden sensation in the face, which follows an operation, before it is made irrevocably permanent. Wilfred Harris is the chief exponent of this form of treatment and in a very large series of cases, he has had many permanent cures. His approach is through the lateral aspect of the cheek and then over the sigmoid notch of the mandible direct to the *foramen ovale*.

Hartel has described a somewhat longer but easier approach, from a point 3 cm. lateral to the angle of the mouth, the needle being aimed at the pupil in the antero-posterior plane, and at the pre-auricular point, in the lateral plane. It should enter the *foramen ovale* at a depth of 5 to 6 cm.

In 1938, Sjöquist (1939), of Stockholm, devised an operation called intra-medullary tractotomy, for the cure of trigeminal neuralgia, especially when the ophthalmic division was affected. In this procedure, portion of the descending root of the fifth nerve is sectioned on the postero-lateral aspect of the medulla. As the pain fibres of the first division are the most superficial, they are the easiest to deal with, and as physiological grouping of fibres has already taken place, the touch fibres are spared.

The incision is made into the *tuber cinereum* in a transverse direction, starting 2 mm. above the lowest root of the vagus, for a distance of 4 mm. to a depth of 3.5 mm.

If the operation is done under local anaesthesia, the extent of the loss of pain sensation produced, can be checked. In some cases, nystagmus, ataxia of the ipsi-lateral arm and leg, and some dysphagia may follow but these disturbances are usually transitory.

Subsequently, Earl Walker (1939) and others devised an operation known as mesencephalic tractotomy, in which the pain fibres of the quinto-thalamic tract are divided in the mid-brain, but the approach is a more difficult one and carries with it more risks of damage to other structures and of haemorrhage.

2. Trigeminal neuritis and post-herpetic neuralgia.

This is an intractable distressing condition and is due to a virus infection of portion of the Gasserian ganglion, usually the ophthalmic division, resulting in *herpes zoster ophthalmicus* appearing some days after the onset of the pains. The other divisions may be involved at the same time or separately.

A true trigeminal neuritis may follow the use of certain hair dyes, and in cases of vitamin deficiencies, especially of the B complex.

In the treatment of the acute stage, large doses of Vitamin B.1, up to 200 mgm. a day, sometimes by intra-venous injections, are indicated. Once the diagnosis of *herpes zoster* is suspected, large doses of chloromycetin and/or aureomycin should be given by mouth for a week. These antibiotics shorten considerably the duration of the blisters, prevent secondary infection and aid healing of the blistered areas.

In elderly people, there often persists, in the affected area of numbness, a continuous insistent pain, a condition called *anaesthesia dolorosa*. It is one of the most intractable pains and may lead to suicide. Any form of attack upon the trigeminal ganglion or its sensory root by surgery, and especially alcohol injections, is contra-indicated and only worsens the pain. Deep X-ray therapy is of doubtful value. On the theory that the pain is associated with a perversion of a local axone reflexive circuit, injections of local anaesthetic solutions into the affected skin and subcutaneous tissues, will often give temporary relief, and if they do, then an operation, similar to Ball's operation for *pruritus ani*, should be undertaken. At this operation, the affected skin is raised up and undercut, and thus denervated, before being replaced, only leaving it attached by sufficient pedicle to maintain its blood supply. This procedure has been tried recently in 3 cases of post-herpetic neuralgia with such relief that all drugs could be withdrawn.

3. Anterior migrainous neuralgia.

Anterior migrainous (ciliary) neuralgia (of Harris, 1936a), is a definite entity, distinct from true migraine and from trigeminal neuralgia, and is characterised by pain in the temple, cheek, eyes and jaws. It is unilateral and accompanied by nausea but not vomiting. It occurs in paroxysms which may last from ten minutes to twenty-four hours. They may come frequently for six to eight weeks, followed by a long interval of freedom, during which a dull ache may persist. There is much lachrymation, and congestion of the eyeball but not teichopsia or hemianopia.

This condition is regarded as a vasomotor disturbance of the blood vessels of the dura, especially the middle meningeal artery, and the pain is referred along the recurrent meningeal branches of the trigeminal nerve. This pain is very similar to that which can be produced by the injection of 1/10 mg. histamine, although the latter is usually bilateral. It can be arrested by trigeminal block, but it is uninfluenced by injection or removal of the stellate ganglion, in contradistinction to certain other hemicranias to be described later. Thus, temporary relief can often by afforded by alcohol injections of the supra- and infra-orbital nerves; and more lasting relief afforded by destruction of the inner 2/3rds of the Gasserian ganglion with alcohol, if a trial injection with novocaine has been successful in relieving an "attack."

4. Neuralgia of vascular origin.

In this form of neuralgia, the pain may be referred to any part of the face, jaws, eyes, or temples.

It occurs in attacks which supervene upon a more chronic type of dull pain, and the chief characteristic features are throbbing and burning. Temporary relief can often be afforded by pressure applied to the main artery supplying the affected area, or by an injection of local anaesthetic around the vessel; and if this be so, then ligature and excision of as much as possible of the affected artery should be performed.

The superficial temporal arteries are the most frequently involved, though in a female patient seen recently with pains in the right side of her lower lip and tongue, excision of portion of the external carotid artery and its lingual and external maxillary branches has afforded great relief. The nature of the pathological condition is not definitely proven, but the affected vessels frequently show signs of arteritis, so that ischaemia of the nerves in the vessel walls is probably a factor.

5. Sympathetic hemicrania.

There has always been much controversy on this subject.

In 1926, Harris stated that it was a fallacy to regard sensory painful impulses as being carried centrally along sympathetic nerve fibres, when trying to explain the pain which persisted after section of the sensory trigeminal root. Yet in 1936(b), he stated that there were other forms of paroxysmal hemicrania, in which the pain probably had a sympathetic origin.

These cases differ from migrainous (ciliary) neuralgia and cannot be reproduced by an injection of histamine nor relieved by Gasserian ganglion block, and this

seems to contradict Loyal Davis' (1936) view, that they are produced by stimulation of efferent fibres of the stellate ganglion which go to peripheral blood vessels, and release a metabolite, which stimulates trigeminal nerve endings.

Tinel (1930) described a case in which pain of a continuous burning causalgic nature, with paroxysmal crises, persisted after section of both the 5th and 7th cranial nerves (the latter being supposed to transmit deep pressure pain sensation) and he maintained that the sympathetic afferent pathways were latent and only capable of being awakened in certain pathological states to transmit severe pain. Such primary recurrent hemicranial neuralgia has been relieved by stellate ganglion block or removal, as described by Harris (1936) and also by Craig (1935) of the Mayo Clinic.

This pain recurs at more or less regular intervals. It is a deeply seated burning, throbbing pain in the temple, cheek, eye, nose or gums; and sometimes behind the ear, at the occiput. It may be associated with other autonomic phenomena such as profuse sweating, lachrymation and nasal congestion. If a trial block of the stellate ganglion with novocaine affords relief, then the diagnosis is confirmed and its removal should be advised.

6. Chronic neuralgia of the face and jaws. ("Atypical facial neuralgia.")

This is another definite entity, distinct from Sluder's neuralgia of the sphenopalatine ganglion. It comes under the heading of "Intractable Pain," and usually occurs in women of reproductive age, but one very definite case has been encountered in a man of 30 years of age.

The pain is often started by a dental extraction. It is persistent, day and night, and affects the cheeks, upper jaws and roof of the mouth more often than the lower jaw. The pain may subsequently spread to the whole of one side of the face or even become bilateral.

It has a burning and deeply boring character and may bring with it flushings and a sensation of swelling. The sudden eloquent postures and anguished expressions of the true trigeminal tic sufferers are never seen, and indeed, the patient's demeanour may well belie his or her protests that "the pain is unbearable and never ceases."

These patients are the happy hunting ground of the surgeon, the rhinologist, the ophthalmologist, and even the unwary neurological surgeon. Dental extractions, antral lavage, antrostomy, turbinectomy, *etcetera*, have all been carried out before the fateful alcohol injection is given. All these destructive procedures are not only doomed to failure, but do further harm by "fixing" the pain and diminishing the chance of suggestive treatment, as these pains are regarded as having a psychical origin, often traceable to some nervous shock. Even the reflex vasomotor disturbances may be secondary to psychalgia and pain of central origin.

If the originating cause cannot be found and removed, say, under light basal narcosis, then the question of prefrontal leucotomy must receive consideration. Much has been written on this method of relief, and the results of many cases treated have been published chiefly by American workers, notably Freeman and Watts (1946), Lyerly (1951), Poppen and Scarff (1949). The last named advocates a unilateral operation, corresponding to the side on which the pain occurs and claims results from this limited procedure as successful as from the bilateral operation. The author's experience with ipsi-lateral leucotomy is limited, so far, to the one male patient, mentioned above, and in whom the result was unsuccessful, after some temporary relief.

Several typical cases of this condition have been encountered during the last 15 years and their histories make interesting, if not very flattering, reading.

The following case was previously presented (Money, 1939) but will repay being repeated here.

A female patient, aged 28, was an attractive, intelligent and highly emotional school-teacher. Her father died when she was very young; her mother married again soon after, and she had been brought up by grandparents. Her early schooling had been received at the hands of a governess and then a tutor; but, becoming unmanageable, she was sent to a convent at the age of thirteen. She had

graduated Master of Arts at the age of twenty-one, and was then appointed sports mistress at a leading girl's school. About this time, after one year's engagement, she suddenly broke it off on her wedding eve, and subsequently became engaged to another man. This had dragged on for six years and seemed to be quite unlikely to mature into marriage.

About eighteen months ago, she developed a violent throbbing in her right ear. This was followed by severe neuralgia in the right side of her face, neck and shoulder. About this time she began to experience peculiar sensations of extreme fatigue, as though she were going "dead" inside, and seemed unable to breathe or swallow. On occasions, the roof of her mouth would become numb. Tickling sensations appeared in her Eustachian tubes and small swellings on her uvula. Following antral lavage, shrill screaming noises developed in her right ear. A severe "cold" produced bilateral tinnitus and dragging pains in the right side of her face. Headaches followed and terrible sensations of pressure in her head. Extraction of impacted wisdom teeth led to a pulling sensation at the back of her neck. Cold and wind increased her discomfort. She had to give up teaching when the pains spread to her throat, and she became nearly "demented." An intercurrent attack of influenza saved her from having her sphenoid and ethmoid sinuses curetted. Vomiting, abdominal pain and numbness in her right leg led to appendicectomy. The caecum had failed to rotate completely, and the appendix was found up near the liver! Only the strongest persuasion was able to prevent her having numerous teeth extracted for "pyorrhoea" which did not exist. After much cross-examination, the unsatisfactory matrimonial situation was revealed. Advice to break this off coincided with "falling for" a tea-planter from the East and a change from school surroundings, after which improvement was slowly but definitely maintained.

7. Costen's syndrome of temporo-mandibular joint strain.

This is the term applied to a group of symptoms which were first described by James Costen (1934), as arising from a temporo-mandibular joint abnormality, when the condyle of the mandible does not take its place normally in the articular portion of the glenoid fossa, throughout the various movements of the mandible. These movements are controlled by the position of the teeth and are related to the bite; and thus if the bite is too "closed," as it often is after total extraction of the teeth and with badly fitting dentures, all the mechanics of this joint and its surrounding muscles are altered by this loss of vertical dimension.

The symptoms of this condition are rather diffuse and bizarre and do not seem to fit in with any of the better recognised syndromes. They consist of a dull pain in the ears, low buzzing tinnitus, made worse by chewing, and a stuffiness in the ears. Neuralgic pains may occur at the vertex, over the eye, in the cheek and into the gums, along with burning and prickling sensations in the tongue and lips. The mouth may become dry and swallowing difficult. The nasopharynx may feel full.

There is usually tenderness on pressure over the temporo-mandibular joints and movements there may be painful, noisy and either limited or excessive.

Patients afflicted with this syndrome for years have usually been submitted to many procedures and operations for its relief without success. They have been told they suffer from "nerves" and thus psychological factors arise which may cloud the issue.

Neurologically, the symptoms are largely dependent upon the close relationship between the temporo-mandibular joint and the auriculo-temporal and the chorda-tympani nerves; whilst alterations in the tension and mechanics of the pterygoid muscles account for the symptoms which arise from interference with the patency of the Eustachian tubes and with swallowing.

Treatment of this syndrome by increasing the maxillo-mandibular vertical dimension is the correct therapeutic procedure. It calls for careful clinical discernment and judgement because, if this dimension is increased too much, or when it should not be increased at all, intense pain and considerable damage to the masticatory apparatus, with loss of bone, may be caused. Usually the increase is accomplished in steps and rarely can a patient tolerate the full change from the original state to the theoretically normal at once; but if the diagnosis and treatment is correct, then partial relief should occur within forty-eight hours of joint rehabilitation and be complete in three to four weeks.

8. Neuralgias due to cranial and extra-cranial tumours (including aneurysms).

Pain in the trigeminal field may be due to any of the above mentioned lesions, owing to the widespread distribution of the 5th

nerve and its branches in the middle and posterior fossae, in the walls of the cavernous sinus and the orbit, and in canals in the base of the skull.

This pain should, however, be readily distinguishable from other neuralgias by its constancy, its increasing severity; and by the finding of anaesthesia or analgesia in the area of pain. Paralysis and wasting of the masticatory muscles on the affected side may be found also. The pain is often accompanied by some ophthalmoplegia or ptosis or proptosis; and neuropathic keratitis may follow.

This type of pain is often one of the earliest symptoms of a naso-pharyngeal growth which has invaded the base of the skull or of a primary cancer of the ethmoid or sphenoid sinuses (Trotter's syndrome).

Acoustic neurinomata, or other tumours of the cerebello-pontine angle, frequently cause pain over the eye and corneal hyperaesthesia before the significance of deafness, tinnitus and vertiginous attacks is realised; and paraesthesia when shaving is another early manifestation.

Meningiomata of the petrous ridge, on the *tentorium cerebelli*, and of the inner portion of the sphenoid ridge and middle fossa have all been encountered. Primary neurinomata of the 5th nerve or Gasserian ganglion may occur, but they are rare and have only been seen twice in the last twenty years. They usually cause complete paralysis and wasting of the muscles supplied by the motor root. Tumours of the pituitary gland may grow into the middle fossa to involve branches of the 5th nerve, and metastatic tumours may occur in this area.

Aneurysms of the circle of Willis or of the intra-cranial portion of the internal carotid arteries, can also cause a lot of pain in the trigeminal area, usually that of the ophthalmic division. These pains may occur in attacks, as the aneurysm increases in size or leaks a litle, but they are very often accompanied by some variety of ophthalmoplegia, and this should distinguish them from true trigeminal tic and true migraine. This is the condition known as *migraine ophthalmoplegique*, and it is only since the advent of cerebral angiography and its wide-spread use, that the true origin of these "attacks" has been discovered.

Following a fracture or severe injury to the base of the skull, an arterio-venous fistula may develop between the internal carotid artery and the cavernous sinus and produce a similar condition.

Finally, localized basal tuberculous or syphilitic meningitis may also involve the 5th nerve and produce much pain in its distribution.

The treatment of all these types of "neuralgia" must, of course, be directed to the removal of the primary cause, where feasible, but often the lesion is inoperable when first diagnosed and then deep X-ray therapy and/or alcohol injections have to be relied upon as a palliative measure only.

9. Neuralgias of central origin.

These are rare cases of neuralgia and where no other cause can be found, they must always be borne in mind. Harris (1950) has drawn attention to the occurrence of a rare form of paroxysmal trigeminal neuralgia which has followed trigeminal neuritis and is an early symptom of approaching disseminated sclerosis. It often occurs when there is an area of sclerosis well established in the medulla.

Thrombosis of the posterior inferior cerebellar artery causes a definite syndrome, due to sclerosis which affects chiefly the spinal root of the 5th nerve.

Infiltrating tumours of the pons, mid-brain and posterior part of the third ventricle, involving the quinto-thalamic and cortico-thalamic tracts, or even the thalamus itself, have all been met with. In these cases, the pain is particularly unpleasant and widespread and often associated with hemianalgesia.

Encephalitis may also cause areas of sclerosis which will involve 5th nerve pathways; and syringo-bulbia is a rarer condition, which has to be borne in mind but which usually has other manifestations.

In all these cases, there is a little or no treatment which can be given to alleviate the cause of the pain and, if severe enough and

leading to drug addiction the question of prefrontal lobotomy should receive serious consideration.

SUMMARY

1. The facial neuralgias form a group of symptom-complexes, characterised by pains of various types in one or both sides of the face.

2. The commonest variety is true trigeminal neuralgia or *tic douloureux*, and it has certain definite characteristics which distinguish it and without which the diagnosis should be reviewed.

3. Eight other varieties of facial neuralgia are classified and described. Some of theses have a definite cause and are associated with tumours or aneurysms around the base of the brain or skull. Others have characteristic symptoms and signs.

4. The treatment of these various conditions is discussed on the following lines:—
   (a) Analgesics.
   (b) Anti-neuritic vitamins.
   (c) Injections of alcohol into the branches of the 5th nerve, its roots or the Gasserian ganglion.
   (d) Resection of the sensory root of the 5th nerve.
   (e) Attack upon the sympathetic nerves or blood vessels supplying the affected area.
   (f) Removal or correction of the cause, when known.
   (g) Prefrontal leucotomy for intractable pain.

5. Migraine and neuralgias of nasal and ocular origin are omitted.

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TESTICULAR TUMOURS

THE ASSOCIATION OF SEMINOMA AND TERATOMA

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" . . . we found that our impulse to dismiss a problem summarily on the strength of an abstract argument *a priori* was checked—as soon as we took our customary precaution of exploring the ground empirically —by an immediate discovery of concrete evidence which showed, in the mere fact of its palpable existence, that our problem was not an empty formality after all."

Arnold J. Toynbee—
The Study of History.

TUMOURS of the testis, differing as they do in many respects from other tumours in the body, present special problems. Some of these are common particularly to tumours of the ovary, kidney and adrenals. The main differences from other growths may be grouped under macroscopic appearances, the histological features and the special nature of the tissues from which the tumours arise, that is to say, their histogenesis. These are sufficiently well known not to require special statement and will be discussed incidentally.

The modern generally accepted view is that there are two main kinds of these malignant tumours of the testis. In view of the very wide agreement regarding this, one is inclined at first to consider that the position regarding them is fixed, at least for some considerable time, and that therefore there is no problem to discuss. However, the evidence of association in one organ of these two kinds of tumours, in several cases, not only indicates that a review of the problem is not "an empty formality" but also demands a careful assessment of their relation and nature.

If the practical man looks at this he may still be inclined to regard it as a theoretical problem of insufficient importance to justify detailed attention. However, the consideration of the cases discussed here shows that there are clinical problems which require elucidation and that some peculiar biochemical "discrepancies," which arise directly from certain *a priori* views as to the nature of the tumours, may be dispelled.

There are three main views regarding the nature of these tumours: (1) that they are both complicated growths and thus are variants of one kind of tumour—the "teratoma"; (2) that they are two distinct forms of tumour: one which is complicated — a "teratoma"—and the other a more simple tumour—a carcinoma which is here given the special name of seminoma; and (3) that both tumours are essentially simple being one or other form of carcinoma.

As mentioned above, the common view is that they are two distinct forms; however, the observation of the relatively frequent combination of the two tumours and, furthermore, the kind and degree of association of these, as well as certain other features which will be mentioned, make it unlikely that they are unrelated. It is the purpose of this paper to show that they are indeed both simple tumours which are comparable with the carcinomata occurring in other organs.

So many of our ideas about these tumours depend on, and incidentally are confused by, the many views that have been expressed in the last century that it is desirable that we should consider them briefly.

Historical Note

The earlier descriptions of testicular tumours emphasized the (uncommon) complex growths and their complexity attracted special attention. This, together with their occurrence in the sex glands, gave rise to the idea of a relationship to monsters; it was an easy step from this to postulate an origin from sex cells (in the sense of totipotent cells which can give rise to new individuals). So there were developed many hypotheses, some of them curiously naïve, depending on the idea of included parasitic individuals.

Most of these hypotheses have long since been shown to be untenable and have been discarded. Although so many have been disposed of, the general idea continues to reappear in some or other form and, of course, is implicit in the term that is applied to so many of these tumours, that is, "teratoma." It is important to appreciate that this idea, impressive one suspects because it is spectacular, still has such an insidious but strong influence on our outlook.

This notion of the monster or the teratomatous growth was so expanded that, as in the case of the ovary, numerous "descriptions" were given of all kinds of organs in the less rapidly growing forms of these tumours. It was perhaps natural that malignant tumours, particularly as some showed heterogeneity of structure, should be regarded as of the same kind.

Towards the beginning of this century attention was given to the group of tumours which differed from the others in that they had a homogeneous structure. Chevassu in 1906 suggested that these tumours arose from cells of the seminiferous tubules and designated this type the Seminoma. These tumours thus now fell into the category of growths of the individual's own cells; the similarity of the tumour cells to each other did not demand a totipotent cell of origin. In passing it should be noted that in recent years the term Dysgerminoma (Meyer, 1931) has been replacing that of Seminoma; this emphasizes that the tumour cells do now show features of the sex cells and also that similar tumours are to be found in the ovary.

Although the group of simple (that is, homogeneous) tumours was recognized by the French school and gradually came to be accepted very widely, there were many pathologists who clung to the older idea that all tumours were fundamentally complex. The discovery of numerous examples in which a mass of uniform structure was associated with one of more complex structure supported this idea. This point of view was propounded very clearly by James Ewing (1919) in his *Neoplastic Diseases*. Largely because of the close intermingling of the typical seminoma with a variety of other tissues it was deduced that all were teratogenous. The homogeneous tumours were considered to arise by "suppression of slowly growing" structures or by overgrowth and destruction of some tissues by one rapidly-developing cell or tissue type. This is clearly a return towards the original view of the monster growing from a sex cell.

To summarize briefly, we see that at first there was the hypothesis of the essential complexity of growths which arose out of confused intermingling of tissues in a few cases, and also from the occurrence of the growths in a region where perennially there occurs the amazing phenomenon of the maturation and growth of the sex cell. An opposing school emphasized the relatively simple nature of some of these (the seminomata) and some writers have placed most of the malignant tumours in a group comparable with tumours of other organs. However, the attraction of the intricate and the involved idea has obviously been very great. It should be appreciated that this emphasis on the sex cell is an unjustifiable insistence on the capacity of a cell to do what ordinarily it is able to carry out only after there have been fundamental changes in it associated with interchange of nuclear chromatin from another cell.

The present position is that, as far as the malignant tumours are concerned, seminoma is now regarded by most investigators as being a simple form of growth, though by a few still regarded as being a "teratoma." As for the remainder, they are considered by the majority as being "teratomatous," though a few investigators consider them as carcinomata.

The association of a "complex" growth (teratoma) with the simpler form (seminoma) has been described by many writers. A good account, with discussion of its significance, has been given particularly by Willis (1948). Scully and Parham (1948) remarked that "although usually seminoma and teratoma are distinct tumors, they may grow side by side or be intimately mixed with each other." This is followed by the remark that "the impure tumor is regarded as teratoma." Although the reason for this is that the "teratoma" carries the graver prognosis and therefore such a view could be justified in a purely clinical approach, it indicates how opinion so commonly veers toward the one direction.

TABLE 1

Case No.	Age	Side	Length of History	Size of Testis in Centimetres	Relation of Tumours	Histological Types	Metastases		End Result
							Site	Histological Type	
1	27	R	2 months	slight enlargement	one type only	Seminoma only	Lymph nodes of neck	Papillary Glandular	(still alive 4 years)
2	28	L	5 months	6 x 4 x 3	M	Glandular Anaplastic	——	——	(alive 3 years)
3	23	L	5 weeks	7 x 5 x 5	D	Glandular Anaplastic	——	——	(alive 3 years)
4	32	L	5 months	8 x 6 x 5	M	Glandular Squamoid	A.L.N.	Glandular Squamoid	3 years
5	28	R	3½ months	7 x 5 x 4	M	Glandular Anaplastic	——	——	(alive 3 years)
6	34	R	9 months	13 x 8 x 8	D	Glandular Anaplastic	A.L.N. Lungs	Anaplastic	3 years
7	36	R	6 months	8 x 6 x 4	M	Glandular Anaplastic	A.L.N.	Glandular Anaplastic	20 months
8	31	L	2 weeks	4 x 3 x 3	D	Papillary Anaplastic	A.L.N.	Glandular Papillary Anaplastic	3½ years
9	21	R	5 months	9 x 5 x 4	D	Glandular Anaplastic	A.L.N.	?	(alive 2 years)
10	35	L	3 months	7 x 4 x 3	D	Adeno-carcinoma	A.L.N. Lungs Liver	Adeno-carcinoma	5 years
11	55	R	6 years enlarging 1 year	6 x 4 x 4	D	Well-formed glands squamoid	A.L.N.	Seminoma Glandular	5 years
12	33	L	7 months	7 x 7 x 4	M	Glandular Anaplastic	A.L.N. Lungs Liver Kidney	Glandular Seminoma	1½ years

This table gives the general features of the twelve cases which form the basis of this paper. The average age at the onset of the condition is 32 years. The tumours occurred equally on both sides of the body. The first symptoms, in all cases except one, was swelling of the testis and in that case (Case 1) there was a swelling in the neck. With the exception of Case 11 there was a relatively short period (average just over four months, if Case 11 be excepted) before the patient sought attention. The relation of the two tumours is given by: M = intermingled or mixed tumours; D = discrete tumours. The histological types refer to the "teratomatous" element. In all cases seminoma tissue was present. The commonest site for metastases was the abdominal lymph nodes (referred to as A. L. N.). In the final column the times referred to are those at which death occurred after the patient had been operated on (with the exception of those given in brackets where the patient is still alive and the length of time since operation is given).

MATERIAL

The specimens which form the basis of this paper were encountered amongst the routine material seen in the Pathology Department of the Royal Melbourne Hospital over a period of several years. There were, however, several other cases which had been sent from other centres for diagnosis and some which had been sent for examination by colleagues who knew of the interest which had been aroused by this association of the tumours in one organ. For these reasons the number of cases of combined teratoma-seminoma encountered is out of proportion to the total number of testicular tumours seen (45 cases), when we consider Willis's (1948) series of 5 cases of combined seminoma-teratoma in association with 21 cases of seminoma and 15 cases of teratoma.

The general features of these tumours are set out in Table 1. The age of the patient ranges from twenty-one to fifty-five years and the average is thirty-two years. The tumours occurred equally on the two sides. With the exception of one case, there was a relatively short history before the patient came for treatment. In all cases except one (Case 1) attention was drawn to the condition by discomfort in or swelling of the testis. Other features of these cases are discussed later.

It is not proposed to give the case histories *in extenso* but three, which show different and characteristic types of association of the two tumours, are discussed in some detail and can be regarded as characteristic of the remainder.

CASE HISTORIES

Case 1.

J.L., aged 27 years, noticed a lump on the left side of the neck just above the clavicle. This was regarded as an enlarged lymph node and ten days later one, now recognized as being only one of a rapidly enlarging group of lymph nodes, was removed for microscopic section.

FIG. I. Photograph of a sagittal section through the right testis of the patient described in Case 1. The organ is only slightly enlarged and there are two irregular masses of homogeneous, somewhat yellowish tissue, in the testicular parenchyma. Histologically all of this tissue showed the structure of seminoma only (see Fig. II). Natural size.

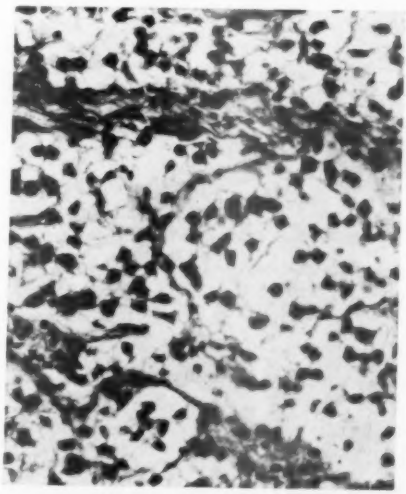

FIG. II. Photomicrograph of a section of part of the tumour shown in Fig. I. The tumour is composed mainly of large cells with clear protoplasm and large rounded or ovoid nuclei. There has been some shrinkage of the cells. In the stroma a few small round cells may be seen. (x 250)

The node was roughly spherical and measured 1.5 cm. in diameter and on cross section had a homogeneous firm texture and was whitish in colour.

Histologically the lymphoid tissue, with the exception of a peripheral rim, is replaced by a mass of epithelial cells which had a mixed glandular and papillary structure (Figs. III and IV). The cells are cuboidal in form and there is some variation in size. Many mitotic figures are present. A diagnosis of secondary carcinoma, the primary growth being possibly in thyroid gland, lung or kidney, was made.

Investigations were now carried out. Examination of the nose and throat, bronchoscopy, X-ray examination of the chest, intravenous pyelogram all failed to reveal any abnormality. Hemi-thyroidectomy and removal of the lymph nodes was carried out but the lobe of the thyroid gland was normal.

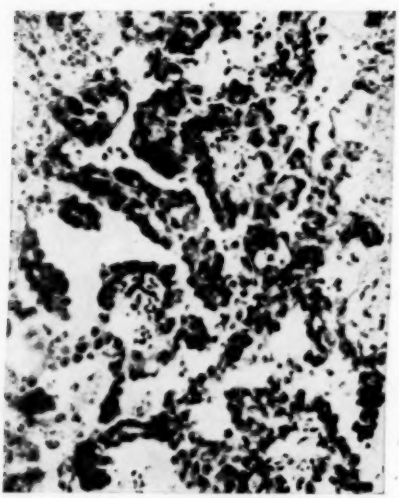

FIG. III. Photomicrograph of a section of part of the tissue removed from the neck of the patient described in Case 1. This shows typical papillary carcinoma (see Fig. IV). (x 120.)

Two months after the first swelling was noticed a slight swelling was noticed by the patient in the right testicle and a little over a week later orchidectomy was performed.

The testis was slightly larger than normal in size and on sagittal section showed two separate irregular masses, occupying the middle portion of the organ (Fig. I). They had a greyish homogeneous structure and serial slices of the organ showed that they were contiguous in one part.

Histologically these are composed of masses of large polyhedral cells lying in a fibrous stroma in which there are a few small rounded cells (Fig. II). The large cells contain a considerable amount of clear protoplasm which is, in some, shrunken and contracted. The relative amounts of large cells and stroma containing the small cells varies greatly in different parts of the section.

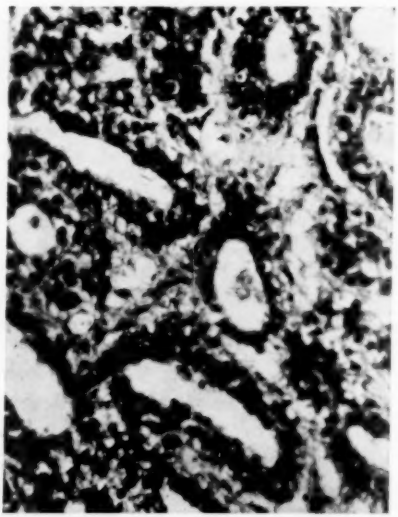

FIG. IV. Photomicrograph of a section of part of the tumour removed from the neck of the patient described in Case 1. It shows a typical malignant glandular structure. In no part of the neck tumour was any tissue resembling seminoma found. (x 200).

Case 2.

J.P., aged 28 years. Some hypersensitiveness of the left testis had been noticed for five months. During the last ten weeks of this period a firm diffuse enlargement of the organ had been noticed and there had been occasional dull aching pain. In the last week increase in size had seemed definite. On examination the testis was only very slightly enlarged and there was a slight, firm prominence of the upper part of the anterior border. Exploration of the organ was undertaken and orchidectomy then performed.

The testis was slightly enlarged, measuring 6 x 4 x 3 cm. and being largely replaced by tumour tissue. This consisted of tissue in which there was some variation in consistency and some areas showing haemorrhage (see Fig. V).

FIG. V. Photograph of a sagittal section through the right testis in Case 5. The testicular tissue is almost completely replaced by a soft tumour which is somewhat heterogeneous in texture consistency and colour. This tumour closely resembled that seen in four of the other tumours but particularly that described in Case 2. Just less than natural size.

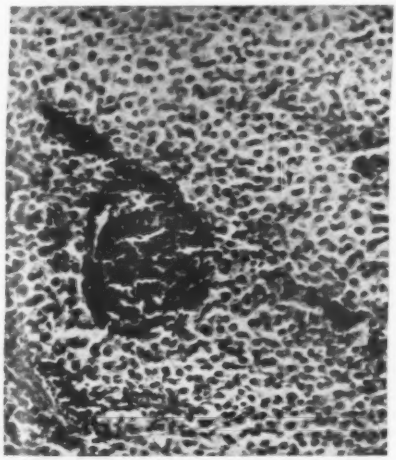

FIG. VI. Photomicrograph of a section of part of the tumour shown in Fig. V (Case 5). Most of the tumour is composed of large cells with clear protoplasm and large ovoid or rounded nuclei. Amongst these there are scattered some small round cells. There is a well-defined nodule in the tissue composed of small cells which, however, are larger than the "small round cells" in the stroma and are arranged in cords and "ducts." (x 150).

Histologically most of the tissue is composed of masses of large polyhedral cells with voluminous protoplasm; amonst these cells there are scattered a few small rounded cells. Although there are some parts of the tumour in which epithelial cells are arranged in groups and cords without any recognizable "seminoma" cells, in many areas there is a mingling of the two types. This interminging occurs as masses of small epithelial cells lying in sheets of the large, pale cells of typical seminomatous tissue. The smaller cells superficially resemble small round cells but are, in fact, larger, contain more protoplasm and are arranged in cords, glands and "ducts" (see Fig. VI). The masses are well defined from the surrounding tumour tissue (Fig. VII).

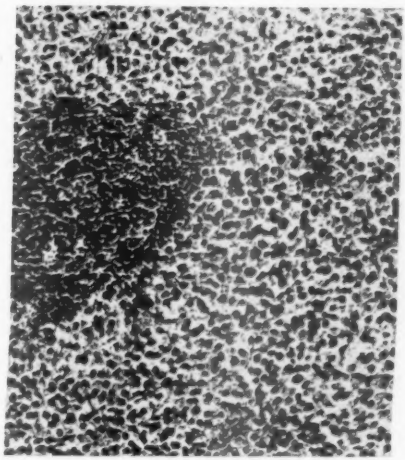

FIG. VII. Photomicrograph of a section of portion of the tumour from Case 5 showing a sheet of large cells with clear protoplasm and large rounded nuclei amongst which there are a few small round cells and (on the left of the section) a well-defined mass of smaller cells which, however, are larger than the small round cells and show an incipient glandular arrangement. (x 150).

Case 3.

H.F., aged 23 years, for five weeks had noticed discomfort in the left testis when walking. There was enlargement of the organ which had been progressive over this period. For the last week of the period there had been actual pain in the testis. On examination there was a smooth enlargement of the organ. Orchidectomy was undertaken.

The testis was enlarged, measuring 7 x 5 x 5 cm. On sagittal section it was occupied almost

entirely by tumour tissue which showed a heterogeneous appearance in most of its extent but in one portion there was a nodule which was uniform in texture and grey-yellow in colour (see Fig VIII).

FIG. VIII. Photograph of a sagittal section of the right testis removed from Case 9. The testicular tissue is completely replaced by tumour which is in the form of two definite masses, the larger one occupying the posterior part of the testis and a smaller rounded nodule in the anterior part which is largely surrounded by, but nevertheless distinct from the former. The main part of the growth was composed of glandular and anaplastic carcinomatous tissue and the smaller growth was a typical seminoma. The appearances here were very similar to those seen in Case 3. (2/3 natural size.)

Histologically the smaller portion of the tumour is composed of masses of large polyhedral cells with voluminous protoplasm lying in a fibrous stroma in which there are many small rounded cells (see Fig. IX). The larger portion consists of masses, strands and cords of cells which are arranged partly in a glandular and partly in a papillary form (Fig. X).

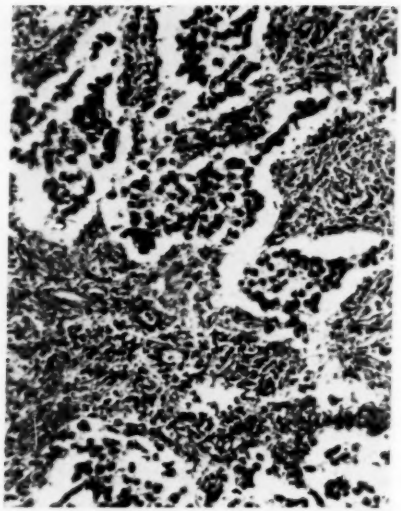

FIG. IX. Photomicrograph of a section of portion of the small nodule in the tumour shown in Fig. VIII. There are small masses of large cells with clear protoplasm and large nuclei of the characteristic type in an abundant stroma in which there are many small round cells. (x 150).

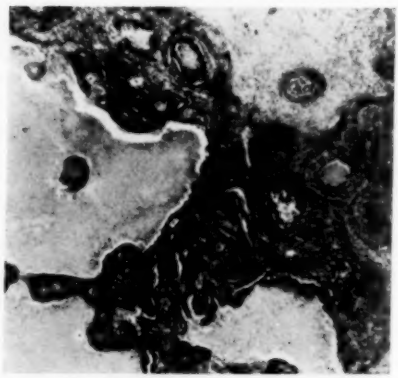

FIG. X. Photomicrograph of a section from part of the larger part of the tumour in Case 9 showing an irregular glandular, cystic and papillary arrangement which is characteristic of tumours described as "teratomata." (x 25).

REVIEW OF MATERIAL

The above cases show three special and different kinds of association of the two kinds of tumour in the testis.

In the first case there is a primary neoplasm which is characteristically a seminoma but in which the metastases, occurring in lymph nodes in the neck, are characteristically and typically a carcinoma, partly papillary and partly glandular. This patient has been observed long enough for it to be clear that there is no other primary tumour in the body. At the same time the testicular tumour was observed at such an early stage that it was possible to examine the whole of it. It can be said therefore with certainty that there is no significant amount of tissue (other than a few cells that may have been overlooked) that does not show the characteristic picture of seminoma. On the other hand the metastases do not show this but demonstrate the other form of epithelial structure.

Such a difference between a primary and a secondary growth is known to occur with many kinds of tumours and, of course, where the two types of epithelium are recognized as being related, some difference in structure between the two is accepted without special comment. Here the clinical course of the condition and the absence of other tumours indicate quite clearly the relation of two forms of epithelium which often are regarded as being unrelated. The clinical importance of the recognition of this feature, where a metastasis is encountered first, requires no special comment.

In Case 2 there was a close intermingling of the two types of tissues. Emphasis has been placed by some writers on the observation of the discrete character and distinct and separate position of the two tumours in many cases. However, in this case, as with several others in this series (Cases 4, 5, 7 and 12) and others which have been referred to by various writers in the literature, there was a very close histological association, the two merging into each other. Some writers are inclined to say that in such cases the seminomatous tissue is only apparently so and is part of the teratoma, but in the cases described here, by every morphological criterion of cell structure, nuclear character and association of small round cells, the material was indistinguishable from that seen in the typical seminoma.

In Case 3 there was the association of the two nodules of different kinds of tissue in the one organ without there being an actual contiguity. Where they appeared to be joining macroscopically, histological examination of this region showed that there was a thin band of connective tissue which separated the two parts of the material so that there was glandular tissue on one side and seminomatous tissue on the other. These were not found in any parts to merge.

Of these three cases, one is unique but the second and third cases resemble, in some degree, the remaining examples of the group. The similarity of the cases actually is close, for example, whereas the case history of Case 2 is given, the specimen from Case 5 is illustrated (Fig. V) as being characteristic of the type. Similarly the specimen from Case 9 (Fig. VIII) illustrates the variety of which Case 3 is the prototype.

One point of special importance is that the "teratomatous" parts of the tumours, in all cases, showed very little variation in structure. Taken together there was a moderate range of cell types but in any example the cell type—glandular or squamoid—was remarkable constant. There was some "undifferentiated," that is to say, anaplastic tissue in most cases but in general the cell range within any tumour was, in these cases, well within that seen in tumours commonly recognized as carcinoma in other organs.

Examination of the tissue at the periphery of the growths showed that appearances, which may be observed in the simple seminomata and "teratomata," could be also seen in these associated growths. In the seminomata, cells morphologically indistinguishable from tumour cells are found at the tumour's edge in the seminal tubules (Fig. XI). In some of these the cells fill the tubules completely but in others they simply line the wall so that a lumen remains. In some areas the cells are uniform in structure, that is to say, they are all of the same kind and closely resemble those of the main tumour. In other parts, however, there are only a few of these amongst the normal cells of the tubules.

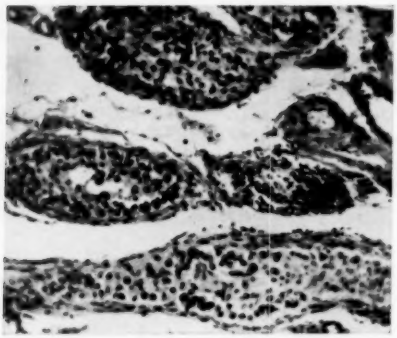

FIG. XI. Photomicrograph of a section of part of the tissue near the edge of the seminoma in Case 6. The testicular tubules contain many large cells which closely resemble those of the tumour. Some of these are presumably tumour cells, but since all gradations can be found between the normal cells and the large cells it would appear that at least some of these are formed *in situ* (see text). (x 150).

These normal cells — spermatogonia to spermatids—in some tubules are typical in structure but in others are larger or have a nucleus-protoplasm ratio different from normal. It has been suggested that these appearances are due to invasion of the tubules by growth and in some cases it seems clear that this occurs; but where gradations can be found between normal tissues and those showing changes in all the tubule cells (as just mentioned) it seems obvious that there is proliferation of the tubule epithelium. The tumour has been growing for some time before these changes occur and the cells described therefore are not giving rise to any part of the tumour, which is, indeed, propagated by proliferation of the tumour cells. What is clear is that cells like those of the tumour can arise from the tubule cells.

This proposition does not need to be discussed at length since the development of these tumours from cells of the tubules is accepted by most pathologists.

Whether the cells of the seminoma correspond precisely to spermatocytes or spermatogonia is a matter of small moment. One common error in contemporary pathological interpretation is the assumption, implicit in many of our statements, that any cell must correspond exactly to some specific known normal cell. If the stimulus acting on a cell be sufficiently different from the normal then it is probable that the result will be something morphologically different from the normal. This is a common observation in many tumours and little is to be gained by straining to find non-existent identities.

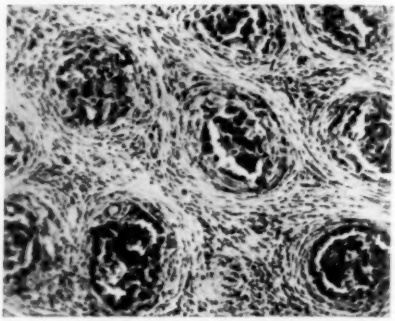

FIG. XII. Photomicrograph of a section of part of the teratoma in Case 9. Here the epithelial cells are in masses around which the connective tissues are arranged concentrically. The epithelial cells are very irregular and atypical in form but they form a striking caricature of tubules. (Cf. Fig. XIII.) (x 110.)

The same sort of observation can be made in some cases of "teratoma," as well as in some of these "teratomata" that are combined with seminoma, and the suggestion immediately arises here as to whether the cells of the tumour are not also of local origin.

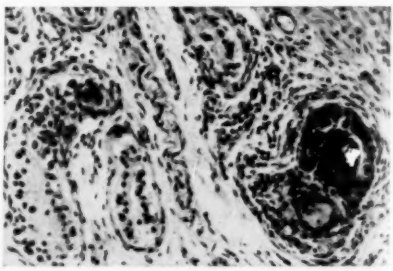

FIG. XIII. Photomicrograph of a section of part of the testis at the margin of the teratoma in Case 10. Here we have the same kind of appearance as in Fig. XI. There are large cells in the tubule (on the left) resembling those of the tumour (on the right) and here again there are gradations to be found between the tubule cells and these large cells resembling those of the tumour (see text). (x 120).

At the margin of a "teratomatous" area (Fig. XII) there are, to be found in tubules, large cells similar to those seen in the main part of the tumour (Fig. XIII). Here there

is the problem also of whether they arise by growth of tumour cells into the tubules. This cannot be answered with complete certainty but several points suggest the origin of the tumour cells in testicular tubules:

(i) the tumour "tubules," despite the different character of the epithelial cells, show the general features of such, that is to say, they suggest caricatures of tubules (Fig. XII);

(ii) gradations can be found between the neoplastic structures and normal tubules (Fig. XIII);

(iii) there is proliferation of the supporting tissues of the wall of the "tubules" such as is seen to occur elsewhere as a response to the presence of an appropriate epithelium.

Furthermore gradations are to be seen between normal cells of the seminal tubules and atypical cells closely resembling those of the tumour.

Here again the proposition is not that cells in testicular tubules seen at this stage, are giving rise to any part of the tumour but that, in view of their morphological similarity to tumour cells, the tumour could have arisen from the cells of such tubules.

DISCUSSION

Most comments made about the association of seminoma and teratoma imply that the two tumours are necessarily different in some fundamental respect. Of course, the typical example of each shows morphological features quite different from those of the other. The seminoma is composed characteristically, on cross section, of homogeneous yellowish tissue whereas that of the "teratoma" has a variegated texture and colour. The differences, however, if they are to be significant, must be deeper and more fundamental than this.

The "teratoma" is generally regarded as a complex growth and therefore necessarily arising from a totipotent or multipotent cell, whereas the seminoma (as with so many other tumours) is composed principally of one kind of cell and therefore is presumed to arise from a unipotent cell. But is such an inference justified? It is important to determine just how complex is a "teratoma" on the one hand and how simple a seminoma on the other. The "teratomata" will be considered first.

As stated previously it was the complex growths which attracted the attention of early investigators. This priority of interest has been maintained and tumours in general are likely to be considered to be more or less simple forms of the "teratoma" rather than being a complicated form of a simple growth. This has applied in the ovary where several tumours have been regarded as being one or other form of "teratoma" and, to take one form of these—the pseudomucinous cyst, it is only after many years that the evidence in favour of its simple origin has come to be accepted.

The "teratoma" arises from some cell or cell group which, apart from the assumed multipotency, is not described. We are necessarily uncertain of the morphological characters of a multipotent cell though, from the many biological examples, it is clear that such characters may be variable and inappreciably different from those of other cells not usually so designated. More telling, however, is whether these tumours do really exhibit evidences of multipotency.

It is important to differentiate between two groups which have been associated arbitrarily—the small group in which the growths contain several well-differentiated and different tissues and the larger comprising the vast majority which shows little variety. Attention is being directed here specially to the second group. As already mentioned these show usually only one kind of tissue and indeed often only one kind of epithelium. The occasional discovery of more than one tissue is seldom greater than is found in many parts of the body where their combined presence, though (and perhaps because) noted frequently, does not call for the diagnosis of "teratoma."

The definition of a teratoma requires some attention. The pathologist may define it as a neoplasm composed of multiple tissues of kinds foreign to the part in which it arises (Willis, 1945). Most of the tumours show very few varieties of tissue and it is pure assumption that these are foreign to the area. This is so only in the sense that any carcinoma is foreign.

The biologist, who looks on an embryo as a self-differentiating cellular system, would define a neoplasm as a cellular system which lacks factors of differentiation. This is a relative matter, however, because the teratoma is a cellular system showing some differentiation in which there is failure of the individuation field. There are many examples of neoplasms in which there is some degree of differentiation. Simple instances include the bone tumours (for example, one containing fibrous, mucoid, fatty, cartilaginous and bony tissue) and carcinomata showing squamous, glandular and mucoid tissues in different parts of the growth. The mixed tumours are more complex examples which nevertheless are not classed with the teratoma. It is clear that, as with many other conditions, the boundary line of the teratomata is an arbitrary one. This somewhat vague boundary is indicated by some more or less generally accepted degree of complexity of the growth. In the case of the testicular tumours under consideration, however, the criteria have been suddenly varied.

In these tumours, there are very few tissues to be found and therefore it is clear that differentiating factors, such as are present in complex growths where the terminology need not be in question, are absent.

If we could be presented with a large series of testicular tumours, without the historical background of the last 200 years, it is almost certain that we would begin with the simpler and much more common growths and proceed from these to the more complex. Attention was drawn to a group of these by Chevassu (1906) and Nicholson (1907) but only this group was segregated from the main body of the tumours which, because of the interest displayed in a few members, were all regarded as complex. Now that embryologists and biologists are demonstrating the fallacies of the doctrines on which the older views were based there is every reason for viewing these growths afresh.

The characteristic of the older views is their rigidity. Despite the everyday observations of remarkable changes in cells as the result of changes in environment, it was (and often still is) thought that any given cell can be related only to one of identical size, shape and general structure and that any such cell will give rise only to cells of a similar form and function. This is well demonstrated in the hypothesis that the relatively uniform character of some tumours is due to one tissue having outgrown and destroyed others; whereas it is a matter of cellular differentiation having proceeded in one direction rather than another.

These problems have been overcome in the case of many of the "simple" tumours. Connective tissue growths often show several kinds of tissue — mucoid, cartilaginous, osseous, fatty, *etcetera*. Nowadays there is no special difficulty in appreciating these as various differentiations of connective tissue. Similarly with epithelial tissues — association of columnar and squamous cells in tumours, for example, of the breast or gall bladder, do not demand special hypothesis.

If we consider a tumour of the breast in which: some of the cells are of the spheroidal type (some arranged in small masses and others in large groups); some are columnar in form with perhaps well-defined gland formation; there is accumulation of cells in ducts as occurs in the duct or comedo-type of carcinoma; an accumulation of mucoid material either in ducts or in the tissues around about epithelial cells, as well as squamous epithelium; their simultaneous presence in the one tumour does not cause us to raise the question of a teratoma. Most carcinomata are simple in form in that only one or two types of epithelia are to be seen, but in almost all parts of the body occasionally a complicated tumour in the sense just mentioned, that is to say, that there are various types of epithelium, is encountered.

In addition to this there are the well known complex tumours perhaps best exemplified by the Wilms tumour of the kidney. Here again we do not demand that they be designated teratoma.

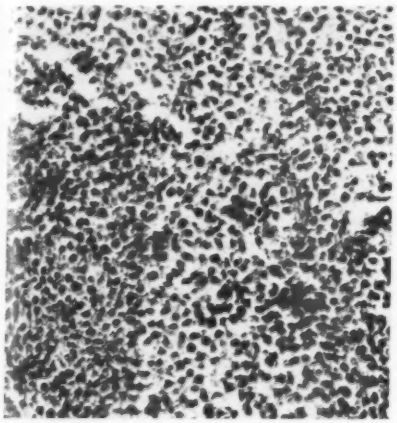

FIG. XIV. Photomicrograph of a section of part of a tumour from Case 4. Most of the tissue is composed of large cells with clear protoplasm and large rounded nuclei. These extend in large sheets throughout most of the tumour and amongst the large cells there are some small round cells. On the left hand side there is a localized, well-defined condensation of cells which are squamoid in form. (x 150).

When a tumour is named, is it a matter of the cell of origin or of the manifest potentialities of the tissue? Actually the first, as yet, we cannot know; as for the second, if there are sufficient different types of tissue the term teratoma is justified but in malignant tumours these potentialities do not become manifest. We have here a special application of the general problem of whether we employ an histogenetic or histological method of classification. As just indicated the former, except in a very general topographical sense, is out of the question, so we should name these growths from the evidence available. Examination of the tumours usually shows only one kind of epithelium; sometimes there are two or three types which in any other part of the body would be regarded as related (Fig. XIV).

The definition of a teratoma given by Willis is that it is composed of tissues which are foreign to the organ; however, we have no more reason for regarding the tissues that we see in a malignant "teratoma" as foreign to the part than we would have for most tumours in other organs of the body.

Regarding the origin of the teratoma from the totipotential cell it must be remembered that evidence is accumulating to indicate that most cells of the body are multipotent. This is indicated by the various types of tumours showing different kinds of epithelia (and even other tissues) mentioned previously. The slowly growing tumours of the testis certainly do show a multipotentiality but it cannot be over-emphasized that one of the outstanding features of malignant "teratoma" of the testis is that usually only a few and often only one potentiality is manifested.

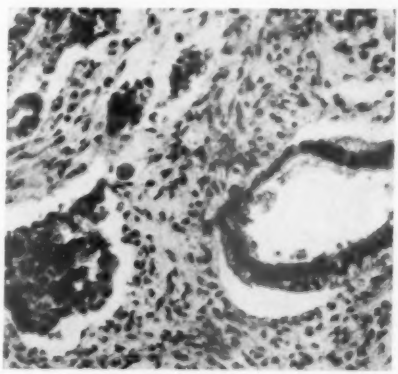

FIG. XV. Photomicrograph of a section of the testicular tumour in Case 12. On the left is a mass of large cells with clear protoplasm and these constituted most of the tumour; however, there were gland spaces lined by a columnar epithelium as shown on the right side. (x 220.)

It has been said that these tumours should be referred to as embryonal carcinomata. This introduces the same fallacy which underlies the general statement that malignant tumours show embryonic characters. The malignant cell is quite different from the cell of the embryo. There are certain similarities depending on the fact that both types of cell are growing rapidly; but the differences are profound. The embryonic cell

is growing in close relation to its fellows and rapidly becomes differentiated to form adult tissues. The malignant tumour cell on the other hand has not the same relation to the surrounding tissues of the individual whatever relations it may have to its immediate fellows and does not form definite organs but shows characteristically the feature of progressive growth.

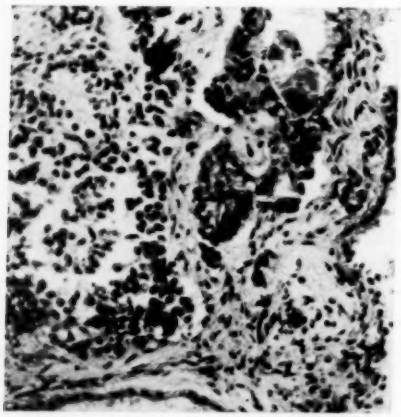

FIG. XVI. Photomicrograph of a section of part of an abdominal lymph node metastases from Case 12. On the left are large cells with clear protoplasm and large rounded nuclei, which constituted most of the tumour, but in this section there are spaces lined by a cuboidal epithelium and a very irregular columnar epithelium respectively. (x 220).

When we look at these tumours from a different angle we see that sometimes in the seminomata there is a development of gland structures which, though ill-defined in form and infrequent in occurrence, nevertheless points to a histological connecting link between the two types of growth (Fig. XV). The close association between seminomatous tissue and carcinoma tissue of other types has been mentioned already and is either given as an argument for the essential teratomatous nature of the seminoma or it is stated that the seminoma tissue is in some way atypical. When all the other features are considered, however, it is apparent that here we have a clear indication of a closer relation between the two types of tissue (Fig. XVI).

One problem of increasing complexity has arisen from the observations made on the excretion of measurable quantities of gonadotropins in the urine. The early results suggested that the follicle-stimulating hormone (probably pituitary in origin) was found, and then thought to occur only, in the seminomata and the luteinizing hormone, biologically identical with the chorionic gonadotropin of pregnancy, was thought to occur only in the teratomata and particularly in the chorion carcinomata.

In cases in which both tumours are present one would naturally expect results which might not conform with those expected from the examination of one part of one tumour; however, in cases where, on exhaustive examination, only one tumour is present contradictory results have also been obtained and it is now generally accepted that morphological appearances of a cell mass may not give a true idea of its physiological capacities. In other words there are biochemical reasons for considering that there may be a close relation between the cells of the seminoma and the "teratoma." Of course, it is to be remembered that, as with tumours in other parts of the body, the cells of either type may have no significant physiological activity.

A great deal has been made of the two kinds of cells in the seminoma—the epithelial cells and the lymphoid stroma. It is not proposed to discuss this here in detail except to point out that the assumption that the small cells are lymphocytes is without adequate justification. Cells very like these are found arising from spermatocytes so that there is no reason for speaking of representatives of two germ layers (as if the epithelium were not mesoderm in any case!). It will be accepted therefore that the seminoma is a "simple" tumour.

It is important that we remember that, in different organs, tumours of the same kind, for example, carcinomata, may show very considerable differences. For example, carcinoma of the thyroid gland is a different kind of tumour from that of the stomach although we recognize them as being essentially similar in their fundamental nature and origin. Differences which are due to the different sites of these tumours are a mask which is likely to conceal their true essential similarities. When we do not allow the knowledge that the sex gland contains cells which, in certain special circumstances,

are different from all the others in the body, to play an unjustifiably predominant role in our deliberations, we can see that all of these tumours are the result of proliferation of cells of the existing adult tissues and none of them arises from some hypothetical totipotential cell. A study of oncology shows that multipotent cells occur in various if not all parts of the body and are not peculiar to any one or few regions. If this is appreciated then there is no need to employ special pathological terms merely for topographical reasons and indeed it is desirable that we use here a terminology which is comparable with that used for other organs.

Even if the name teratoma must be retained temporarily for the well-differentiated growths it should be discarded for the malignant tumours. Such a growth should be regarded as a carcinoma or if necessary (though it is doubtful if the necessity arises) as a complex carcinoma.

The occasional (almost rare) presence of cartilage and bone is usually cited as evidence for a totipotent cell of origin. These can be reasonably regarded only as indicating a multipotent cell but in any case recent observations on the embryology of the jaw and the pathology of "mixed" tumours of the salivary glands and other organs greatly diminish any special significance that previously such tissues may have been considered to possess.

It is reiterated that most of the rapidly growing "teratomata" show no greater variation than do tumours such as some of those mentioned above. Even when peculiar cell masses occur, these are not numerous in type and can be explained usually in a manner which is acceptable, usually without question, in tumours elsewhere.

The idea that these tumours are teratomatous does nothing to help us understand them and has been imposed on us by the weight of the philosophical misconceptions of our predecessors. On the other hand if we accept the simpler viewpoint most of the tumours become merely variants of a simple type comparable with epithelial growths in other organs. It should be noted here that some workers have sustained this point of view and have not been influenced by the spectacular facade of the "teratoma."

CONCLUSIONS

The two main tumours of the testis, one generally recognized as simple in form and the other as a complex growth, are often closely associated.

They occur together in the same organ sufficiently often to indicate that this combination is more than a random relation. In addition to this, in some cases the association is so close and the intermingling of the two kinds of tissue so intimate that some close affinity is manifest.

These two tumours therefore must be regarded either as comparably complex in structure or equally simple and indeed the "teratoma" is usually much more simple than terms that have been applied to it would suggest.

There are clear indications that both the tumours arise from the cells of the tubules.

Tumours of the testis present difficulties greater than those associated with tumours of other organs principally because of a pre-conceived notion regarding the origin of these growths from some peculiar hypothetical totipotent cell in a sex organ.

When we consider the available evidence *de novo* there are no intrinsic difficulties in the acceptance of the term carcinoma for that malignant tumour which differs in structure from the seminoma. We thus have the same kind of terminology as, for example, in the malignant liver tumours — hepatoma (for those closely resembling the parent tissue) and carcinoma (for those resembling other forms of growth). In the testis there is the seminoma, the cells of which resemble in some degree certain of those of the tubules, and the carcinoma, which may have a glandular, papillary or anaplastic form.

SUMMARY

1. Twelve cases of tumour of the testis in which there was an association of a seminoma and a "teratoma" are discussed and three of these are described in detail.

2. The malignant "teratomata" do not usually show a degree of multi-differentiation greater than is seen in many carcinomata in other parts of the body but usually show only an epithelial tissue and often only one form of this.

3. The evidence for the opinion that these are really teratomata is therefore of the slenderest, and the reasons for considering that they are not so are discussed.

4. These tumours (both the "teratoma" and the seminoma) are regarded as arising from the cells of the testicular tubules.

5. The term teratoma, by definition, should be applied only to such tumours as show considerable multi-differentiation and the term should cease to be used as applying to those in which this is not true. For this reason it should not be used for those malignant forms of epithelial growth which differ from the seminomata.

6. Tumours of this kind should be designated carcinoma.

7. The seminoma is a carcinoma but, in view of its characteristic features, this or some comparable term should be retained at present.

8. In this way over 95 per cent. of the growths of the testis, which constitute the malignant epithelial tumours, would fall into two sub-groups, the carcinoma and the seminoma.

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PIGMENTED BASAL-CELL TUMOURS OF THE SKIN

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Department of Pathology, University of Melbourne

Speed. Why, man, how black?
Launce. Why, as black as ink.
The Two Gentlemen of Verona,
Act. III, Sc. 1, l. 289.

It is often thought that because a tumour of the skin contains non-haematogenous pigment, it is necessarily a melanoma. That tumours containing blood (haemangiomata, vascular neoplasms and others containing pigment of haematogenous type) present clinical difficulties in differentiation from the first group is generally recognized. However, these are easily segregated pathologically by the demonstration of iron (Prussian blue reaction) in those containing blood or blood derivatives, or the impregnation of melanin containing structures with silver salts in the remainder.

It has only become appreciated gradually, however, that the epithelial tumours of the skin—squamous papillomata, squamous carcinomata and basal-cell tumours—may also contain non-haematogenous pigment. Accounts of them are to be found in the writings of the last twenty-five years, including some modern text-books of pathology (Muir, 1951), but they are still not given adequate attention.

The importance of this group of pigmented epidermoid tumours is their distinction from the melanotic growths. The amount of pigment in the former group may be sufficient to become a problem for the clinician as well as the pathologist.

Of the various skin conditions, basal-cell tumours were separated arbitrarily from hyperplasias, papillomata and carcinomata in order to limit the scope of this investigation. Concurrently and incidentally, however, and from the same sources, both benign and malignant melanomata were also collected to assess the significance of possible confusion between these and pigmented basal-cell tumours.

In this series the material investigated was from specimens examined in routine fashion at the Pathology Departments of the University of Melbourne and the Alfred, Austin and Royal Melbourne Hospitals over a period of twenty years.

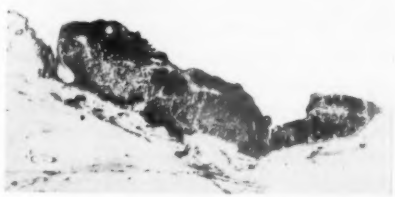

FIG. I. Photomicrograph of a section of a large basal-cell tumour from the back (Case 23) showing extreme degree of pigmentation. The pigment is in dense masses scattered irregularly through the growth. Haematoxylin and eosin. (x 6.)

When the basal-cell tumours in the present group were being examined it was appreciated that some had only a small or even minute amount of pigment. The criteria for a line of separation provided some difficulty but it was decided, as a demarcating line of practical value, to accept as pigmented only such tumours as those in which pigment could be found by simple examination of a routine haematoxylin and eosin stained section. Actually although a small amount of pigment is present in a large proportion of

basal-cell tumours this requires special staining methods for its demonstration. The percentage of pigmented tumours found may be increased in some degree if biopsy be taken specifically from a pigmented area.

SOME GENERAL CONSIDERATIONS

There are various problems relating to the origin of the pigment and to the nature and morphogenesis of the pigment-producing cells which deserve comment.

Melanin.

The pigment concerned in these tumours is a melanin which does not differ in any known way from those found generally in the body. It gives all the usual chemical reactions; it does not give the Prussian blue reaction for iron but is easily impregnated with silver solutions. The melanin granule itself is a highly complex aggregate, not only of pigment but also of at least three enzyme systems, in a protein matrix. Its distribution in man is similar to that in other vertebrates and most invertebrates. The places in which melanin is found are all either ectodermal in origin, such as epidermis, hair, mucous membranes and medulla of the adrenal gland or are tissues the origin of which, though still debatable, is probably ectodermal, for example, the iris and choroid of the eye and the leptomeninges (Du Shane, 1948). Melanin is also found free, though usually only in small amounts, in the connective tissues of the dermis.

Origin and Formation. The development of pigment in a cell is a complex biochemical process which is, as yet, not fully understood. In the pigment-forming cell the melanin pigments occur as granules, usually round or oval and of uniform dimensions. The melanin itself is probably derived from tyrosine or a closely related substance by a series of reactions similar to the dopa reaction. In certain cells, destined to become pigmented, dihydroxyphenylalanine is converted into a brown melanin-like substance through the action of one or more enzymes (dopa-oxidase, tyrosinase).

Originally it was thought that any cell containing melanin had produced its own pigment but now it is known that, among the cells which contain pigment, only some actually produce it; these are designated the melanoblasts. The other cells which contain pigment, without actually having produced it, are melanophores or chromatophores.

Normal skin shows pigment in four sites:

(i) In the basal cells which are the most heavily pigmented.

(ii) In the more superficial cells of the epidermis the pigment being less in amount towards the surface.

(iii) In melanoblasts which are dendritic cells found lying between the cells comprising the deeper layers of the epidermis.

(iv) In the dermis contained in phagocytes as coarse, various-sized granules.

Dawson (1946) and Lennox (1949) use the term melanophage for these phagocytes in preference to the etymologically correct but confusing term melanophore. This terminology will be followed in this paper.

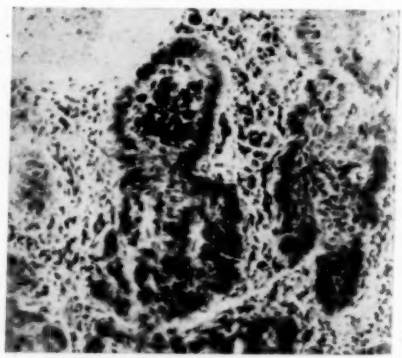

FIG. II. Photomicrograph of a section showing cell masses with pigment granules in and between the tumour cells. Some pigment may be seen in the connective tissue stroma. Haematoxlyin and eosin. (x 150.)

The only dopa-positive cells in the skin are the dendritic cells of the epidermis. Bloch (1927), who first demonstrated the dopa reaction surmised that all the basal cells were dopa-positive but, as the technique of the reaction was improved, this was proven false. Silver impregnations or the

dopa reaction are necessary to demonstrate the dendritic cells and their processes in sections. It has been noted that the more heavily pigmented regions show smaller members of dendritic cells but this is explained by the premiss that the pigment with which the basal cells are loaded conceals most of them.

Argument still centres round the question of whether the epidermal cells themselves can produce pigment. Thus Dawson (1925), Willis (1948), and Bonser (1948) all assert that they do so; Masson (1948) and Becker (1948) assert that they do not. While there is no *a priori* reason why they should not, neglecting for the moment a negative dopa reaction, experimental evidence is accumulating that places the emphasis of the capacity to produce melanin on melanoblasts which thus would be the only cells actually to produce melanin. This evidence conforms with the neural crest theory for the origin of pigment-forming cells (Du Shane, 1943, 1944; Rawles, 1948).

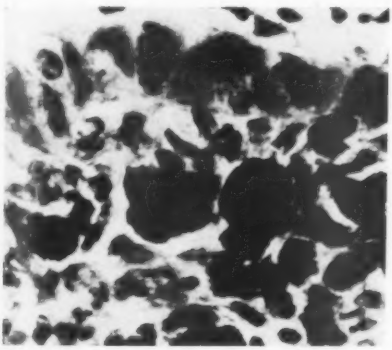

FIG. III. High power photomicrograph of a group of tumour cells showing large amorphous masses of pigment together with pigment granules actually in the tumour cells. Haematoxylin and eosin. (x 700.)

Borcea (1909) reported that migratory cells in the embryos of several species of bony fish detached themselves from the junction of the neural tube and epidermis to migrate either laterally between the somites, or ventrally between notochord and somites. This migration has also been observed in amphibia (Du Shane, 1948; Stearner, 1946), in birds (Rawles, 1945; Willier and Rawles, 1940), though, in mammals, the evidence for the neural crest origin of pigment cells is not as yet conclusive. However, Rawles (1940) found that neural crest cells from mice, grafted to the coelom of a chick embryo, developed pigment in that area, a result in harmony with the neurol crest hypothesis.

With regard to the pigment in the dopa-negative cells of the epidermis, Stearner (1946) has produced evidence to support an observation made originally by Ehrmann (1885). He described streaming of pigment within pigment cells and the transfer of pigment granules to the epidermal cells of freshly prepared frog skin. Stearner observed that the processes of epidermal pigment cells in *urodele* amphibians actually enter the epithelial cells and that there was a close correlation between the presence of epidermal melanoblasts and the melanin present in epidermal cells.

Again in a series of animals in which neural crests of other species had been implanted, it was observed that where the graft melanoblasts failed to enter the host epidermis, no melanin granules occurred in the epidermal cells. These results taken in conjunction strongly suggest that melanoblasts pass melanin granules to the epidermal cells.

REVIEW OF LITERATURE

The earliest reference to pigmented basal-cell tumours appears to be that of Pollio (1906), quoted by Stewart and Bonser (1948). He described three histological types of pigmented tumour in a case of von Recklinghausen's disease, his last group comprising pigmented spots without cell nests but with hyperplasia of the *rete malpighii*.

Touraine (1935), when collecting 42 cases from the literature, described a group of plaster casts made in Paris between 1875 and 1919. Three of these were pigmented basal-cell tumours.

Chambers and Stokes (1927), Bloch (1929) and Pardo-Castello (1929) each presented cases in which pigmented skin lesions had been present for some years. All of these histologically showed the structure of basal-cell tumours with various amounts of pigment present. Pardo-Castello, in particular, stressed the relative benignity of the lesion compared with a malignant melanomata.

Montgomery (1929) drew attention to the pigment occasionally present in basal-cell tumours and demonstrated the sites of the pigment in several cases, using a silver impregnation, in basal-cells of the epidermis, in dendritic cells, and rarely, in the tumour cells. Owen (1930), in a series of 836 basal-cell carcinomata at the Mayo Clinic, noted 7 pigmented tumours.

Ewing (1930), during a discussion of problems of the melanomata, recognized pigmented basal-cell tumours and commented on the occasional difficulty in differentiating them from each other. He pointed out that the pigment cells in the epidermal tumours do not exhibit any neoplastic quality.

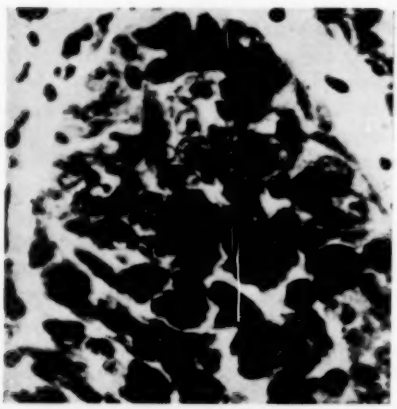

FIG. IV. High power photomicrograph showing pigment in a group of tumour cells. No dendritic melanoblasts can be recognized here. Haematoxylin and eosin. (x 700.)

Eller and Anderson (1933) recorded two cases in both of which, macroscopically, the tumour was pigmented and microscopically showed the typical structure of a basal-cell carcinoma. In both cases most of the pigment was held in the melanophages of the tumour's stroma. These authors emphasized that absolute differentiation between a pigmented basal-cell tumour and a melanoma can only be made on histological grounds. They also mention the occasional confusion between seborrhoeal warts or pigmented papillomata and the melanomata and, as will be mentioned, present experience bears this out strongly.

Becker (1934), using a silver impregnation in a series of 85 basal-cell tumours, including mixed and intermediate forms, found that 27 per cent. were pigmented forms. He discussed the origin of the dendritic melanoblast in these tumours and considered the regularity in size and arrangement of the pigment granules to indicate that the pigment cells are not themselves neoplastic. Gaté *et alii* (1937) found an incidence of 6 to 10 per cent. of pigmented forms.

FIG. V. Photomicrograph showing pigment distributed diffusely both in tumour cell groups and connective tissue stroma. Fontana silver impregnation counterstained with Light Green. (x 150.)

Bonser (1946) pointed out that the whole group of epidermal pigment forming tumours was not well recognized by English pathologists. She stated that the prognosis and treatment of these tumours is exactly the same as for the non-pigmented forms and quite different from that of the melanomata.

Khanolkar (1947) described 11 cases of pigmented basal-cell tumours, two of multiple pigmented basal-cell tumours, and two pigmented squamous cell carcinomata. All his patients were Indians. He stressed the necessity for histological diagnosis, as well as their relatively benign course and discussed the role of melanoblasts in the evolution of these tumours.

Stewart and Bonser (1948) reviewed the literature collecting 57 cases of pigmented basal-cell tumours. In recording their own series of 57 epidermal melanin-forming tumours they include 28 basal-cell tumours. Some 12 of these showed keratinization in some degree. Their series was obtained from routine material stained with haematoxylin and eosin but they do not give the total number of basal-cell tumours examined. They consider the appearances show that the tumour cells form the pigment.

Willis (1948) mentioned pigmented tumours as a link between the ordinary skin tumour and the melanoma and suggests that their existence is evidence for the epithelial origin of melanin.

Teloh and Wheelock (1949) mention that they found 6 pigmented tumours in a series of 182 basal-cell tumours.

Recently Lennox (1949) has reviewed the evidence for the neural crest origin of pigment, concluding that pigment in the basal-cell tumours was produced only by the dendritic melanoblasts; using a modified Masson silver impregnation he was able to demonstrate pigment in 47 out of 124 basal-cell tumours.

DATA

The term basal-cell tumour is applied in this paper to all members of a general group of epidermoid neoplasms in which the cells are epithelial in character, are small in size and are usually arranged in masses, at the periphery of which the outermost cells are arranged in a palisade or "columnar" manner. There is usually absence of any squamous differentiation such as prickle-cell formation or cell nests (though occasional examples may be found in some part of them).

The investigation involved the examination of 1,780 predominantly basal-cell tumours together with 650 melanomas, the second group including both benign and malignant forms. Among these 2,430 sections were found 66 pigmented basal-cell tumours and also, rather surprisingly, 29 seborrhoeic warts.

The percentage of pigmented forms in this series (3.7 per cent.) is low when compared with those of Becker (1934) and Lennox (1949) but these investigators used silver impregnation in screening their tumours, whilst in the present group only haematoxylin and eosin stained sections were used, silver impregnation then being employed to demonstrate the dendritic melanoblasts and other pigment-containing cells.

Clinical details of the tumours, where available, are summarized in tabular form.

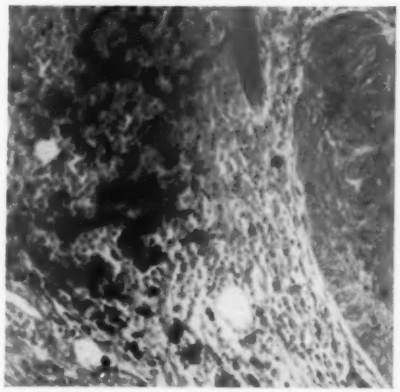

FIG. VI. Photomicrograph showing pigment present in dermal melanophages (in the connective tissue); a tumour cell mass without pigment is seen on the right side of the section. Fontana silver impregnation counterstained with Light Green. (x 150.)

An attempt was made to classify the tumours histologically into six types, on a purely descriptive basis, thus:

(1) Large cell masses.

(2) Sudoriferous differentiation (of type 1).

(3) Column formation or small cell masses.

(4) Reticular type (either large or small cell masses).

(5) Cystic form (usually of type 1).

(6) Mixed basal squamous (basi-squamoid) growths.

Other subgroups could be described but no example of these examined in this series contained pigment. This grouping, since the various types merge, is only an indication of the predominant structure of the tumour.

The amount of pigment present histologically was graded into:

(i) a small amount, in which occasional granules were found;

(ii) a moderate amount, in which pigment was readily observed on casual observation;

(iii) a large amount, where pigment was an arresting or predominating feature. These three groups are represented in the tables by +, ++ and +++ respectively.

The age incidence is maximum in the sixth decade, no tumours being encountered under the age of 25.

Colour was often not recorded. Black and brown were most commonly noted while the phrase "flecks of pigment" occurred frequently in clinical descriptions of the tumours.

As far as could be ascertained, none of these tumours has recurred though several deaths have taken place due to unrelated intercurrent disease. Some patients after adequate removal of one tumour have, several years later, developed another basal-cell tumour in a different site.

Treatment adopted was either surgery or radiotherapy, the second being used often after biopsy of a small section of the tumour. Several tumours were noted as somewhat radio-resistant.

In practically every case, pigment was present both in melanophages of the stroma (Fig. VI), and the epithelial tumour cells, the pigment being in the form of granules of different size (Figs. III and IV). In many sections dendritic cells could also be seen (Figs. VIII, IX and X) lying between the tumour cells and showing small regularly sized granules of pigment. These cells were seen best under the oil immersion lens and in silver impregnated specimens. The distribution of the pigment throughout any given tumour varied considerably. In many, particularly those which were heavily pigmented, the pigment was spread diffusely through all parts of the tumour (Fig. VII is a good example), whilst in others the pigment was confined to one or two small areas.

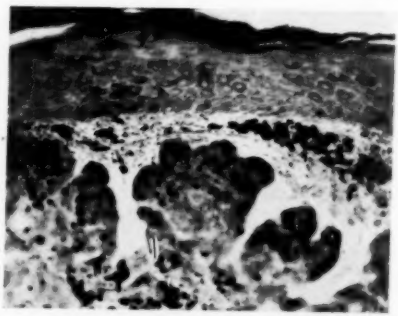

FIG. VII. Photomicrograph showing a large quantity of pigment in the dermis immediately beneath the epidermis. An appreciable amount is also present in the tumour cell masses. Fontana silver impregnation counterstained with Light Green. (x 150.)

DISCUSSION

It will be seen from the above data that the age, sex and site of these pigmented basal-cell tumours are those typical of basal-cell tumours as a whole. Touraine (1935) considered that pigmented basal-cell tumours showed no proclivity for any given site but, in Stewart and Bonser's series, they were much more common on the head and neck, and in the present group 77 per cent of the tumours arose from skin above the clavicles.

There is general agreement that the prognosis is exactly the same as that of the non-pigmented types. It is noted that the heavily

pigmented tumours all ran a course of years and are slow growing. Type 2 on the head and neck was most heavily pigmented. Type 4 (reticular type) was not commonly pigmented, ulcerated early and histologically did not show a clearly defined border of growth.

The patient's presenting complaint was usually that of recent increase in size or ulceration.

Some authors regard the presence of pigment in the tumour cells as being due to proximity to the epidermis, the more superficial portions of the tumour then being more pigmented (Gaté *et alii*, 1937). These authors observe that pigment is absent in an ulcerated tumour. No evidence to support either of these viewpoints has been found in this series but the last observation may be explained partly in that heavily pigmented tumours are slowly growing and ulcerate late.

FIG. VIII. High power photomicrograph of part of a mass of tumour cells showing several dendritic melanoblasts with processes passing between these cells. Their long processes are well demonstrated. Fontana silver impregnation counterstained with Light Green. (x 700.)

An argument which arises here is that, occasionally, the clinician will note flecks of pigment in the tumour and may even take his biopsy specifically to include the pigment; yet on histological examination no pigment is found. The explanation here may be either that the pigment is not melanin, but blood in dilated vessels or a small haemorrhage, or that the pigment is, in fact, melanin but is in the overlying epidermis and not in the tumour itself. It is in the second case that the pigment may disappear when the tumour ulcerates.

Keratinization was not uncommon, occurring in types 1, 2, 3 and 6. It was not seen in type 4. Often the cell nests showed melanin granules.

With regard to diagnosis, although in many cases the lesion was noted clinically to have only flecks of pigment, in an appreciable number of instances the clinical diagnosis of melanoma or malignant melanoma was made. This applied particularly where a pigmented lesion had recently ulcerated or increased in size. This demonstrates very clearly the importance of general recognition of this group of pigmented basal-cell tumours.

Furthermore, in three instances the histological diagnosis of malignant melanoma was made, while in two other cases the lesion was reported histologically as a melanoma. These erroneous diagnoses indicate that there is confusion between the melanomata and the pigmented basal-cell tumours. This confusion, however, was even more obvious in the case of seborrhoeic warts or acanthotic moles.

Among the 2,430 basal-cell tumours and melanomata examined were found 29 seborrhoeic warts; 12 of these were diagnosed as benign melanomata, 14 were diagnosed as basal-cell tumours, 2 as malignant melanomata and one as a basi-squamoid carcinoma.

It is important that this obvious confusion be resolved, since the prognosis of the pigmented basal-cell tumour is uniformly good provided local excision or radiotherapy is adequate. This applies also to the seborrhoeic wart which is seldom, if ever, malignant. The prognosis of malignant melanomata is bad.

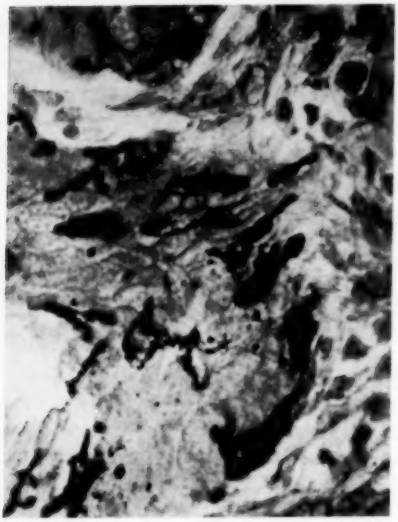

FIG. IX. High power photomicrograph of the margin of a tumour mass showing dendritic cells present amongst the tumour cells. Granules of pigment are also seen in and around the tumour cells. Fontana silver impregnation counterstained with Light Green. (x 700.)

The distribution of the pigment in the tumour varies considerably from one portion of the tumour to another but there are four main sites:

(i) The tumour cells may contain coarse granules of pigment which differ in size (Figs. III and IV), their colour being anything from golden to dark brown. Becker (1948), curiously enough, stated that "the tumour cells contained no pigment although histiocytes often contained large amounts of melanin."

(ii) The dendritic melanoblasts contain pigment distributed in diffuse homogeneous dark brown, evenly sized granules in both cytoplasm and dendrites.

(iii) Melanophages in the stroma contain irregularly sized granules of melanin which may also lie free in the stroma.

(iv) Pigment is very commonly found in cystic spaces away from the periphery of cell masses, this applying particularly to Type 1. The pigment lies free as large globules amidst debris of necrotic material consisting mainly of keratinized bodies of epithelial cells which can not be eliminated in the normal way by being cast off from the epidermis (Khanolkar, 1946).

Wolff (1948), in a discussion of the histogenesis of melanomata, drew attention to the work of Smith (1925) who, by an examination of the pigment granules, differentiated between cells which actually produce pigment and those which take in pigment as a foreign body. The pigment granules, when produced in the cell, are always approximately the same size, shape and colour but when taken in as foreign particles the granules are found in masses which vary greatly in size and shape.

Appearances in the present group of tumours conform with Smith's observations, that is to say, the cells of the tumour produce pigment but only one type of cell is responsible for production, the pigment being then passed on to the other tumour cells.

This specialized cell is the dendritic melanoblast and, in common with Lennox (1949), it was found in the present series, that in small, lightly pigmented tumours they were not easy to demonstrate, whilst in deeply pigmented tumours they were obscured to some degree by the amount of this pigment.

These dendritic cells are found amongst the tumour cells (Figs. VIII and IX) and appear to move away from the periphery as the tumour lobule increases in size. The dendritic cells still retain a connection with the periphery of the cell mass by means of long dendrites, which contain granules of pigment (Fig. X). The cells degenerate, to some degree, as they approach the middle of the lobule and may be extruded into the necrotic material in the cystic space which is often present. The pigment in the melanophages is probably obtained by phagocytosis after extrusion from the cell masses.

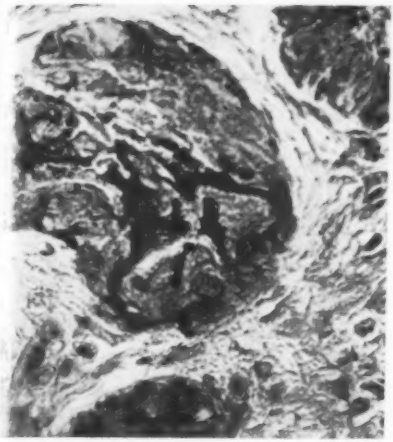

FIG. X. Photomicrograph of a section showing a small tumour cell mass through which dendritic melanoblasts are to be seen among the tumour cells. Processes of the melanoblasts are seen to contain pigment (see text). Fontana silver impregnation counterstained wth Light Green. (x 700.)

It has been suggested (Tod, 1946) that irradiation could be used as a diagnostic test of pigmented tumours of the head and neck; that if after radiotherapy a distinct patch of pigment remains the tumour is a melanoma but if there is no pigmentation left it is an epidermal tumour. Becker (1948) and Kaye Scott (1952) have demonstrated this test to be fallacious since they found that, after efficient deep therapy to a pigmented basal-cell tumour, pigment may still be left.

It is realized that pigmentation in these tumours must be more common than actually found in this series where only sections stained with haematoxylin and eosin have been screened and of necessity, only a part of the tumour has been examined.

It has been suggested that we would expect a vastly greater proportion to be pigmented if the basal cells themselves actually produced the pigment (Eller and Anderson, 1933), but it is probably still too early in our knowledge of this complex subject for us to be able to make far-reaching deductions from our still imperfect and incomplete observations.

CONCLUSIONS

Pigmentation in basal-cell tumours is simply an extension of normal pigment production as it occurs in the skin. The predominant pigment producing cells appear not to be neoplastic. Pigment is to be found in the tumour cells. The immediate practical significance of the recognition of these tumours lies in the danger of confusing them with the melanomata.

SUMMARY

A series of 1,780 basal-cell tumours and 650 melanomata has been examined histologically using haematoxylin and eosin stains for the original routine examination.

A group of 66 pigmented basal-cell tumours is recorded and classified.

The origin and formation of melanin is discussed. Dendritic melanoblasts can be demonstrated in these tumours and are considered to be at least mainly responsible for the formation of pigment which is then passed on to the epithelial cells of the tumour.

The pigmented tumours behave in the same way as the non-pigmented otherwise comparable tumours and their practical importance is their differentiation from melanomata. It is shown that there is confusion between these two groups of tumours.

The available literature of pigmented basal-cell tumours is briefly reviewed.

ACKNOWLEDGEMENTS

I wish to express my sincere thanks to Dr. R. Kaye Scott, Dr. J. D. Hicks, Pathologist to the Royal Melbourne Hospital, Dr. A. V. Jackson, Pathologist to the Alfred Hospital, and Dr. R. Motteram, Pathologist to the Austin Hospital, for assistance in this investigation.

TABLE 1

Summary of the clinical and histological features of the 66 cases which form the basis for this paper.

No.	Sex	Age	Site	Size	Duration	Histological Type	Amount of Pigment Histologically	Pigment Distribution	State of Epithelium	Comment
1	F	74	face	5 mm.	4 years	2	+++	diffuse	intact	Queried as "melanotic sarcoma" clinically
2	M	53	cheek	5 mm.	3 years	3	+	local	ulcerated	
3	F	59	nose	6 mm.	—	4	+	local	ulcerated	
4	F	—	cheek	6 mm.	2 years	1	+	local	ulcerated	
5	M	30	back	20 mm.	6/12	1	+	diffuse	ulcerated	Queried as fungating pigmented mole clinically
6	M	58	scalp	10 mm.	—	3	+	diffuse	ulcerated	
7	F	54	neck	—	10 years	4	++	diffuse	ulcerated	Mole ? melanoma clinically
8	F	56	nose	8 mm.	2 years	4	++	local	intact	Pigment noted clinically
9	M	48	buttock	30 mm.	10 years	3	++	local	ulcerated	Pigment noted clinically
10	F	79	nose	8 mm.	15 years	3	+	diffuse	—	
11	M	—	nose	—	4/12	2	+	local	ulcerated	
12	M	56	chin	20 mm.	12 years	3	+	diffuse	intact	
13	F	57	nose	12 mm.	15 years	3	+	diffuse	—	Pigment noted clinically
14	M	—	nose	3 mm.	9/12	1	+	diffuse	ulcerated	Pigment noted clinically
15	F	70	forehead	10 mm.	18/12	3	++	local	—	Pigment noted clinically
16	M	50	cheek	7 mm.	life	3	++	diffuse	ulcerated	Pigment noted clinically
17	M	69	eyelid	15 mm.	years	1	+	local	intact	
18	M	78	cheek	25 mm.	years	5	+	local	ulcerated	Pigment noted clinically
19	F	44	temple	6 mm.	10 years	4	+	diffuse	ulcerated	
20	M	63	nose	20 mm.	—	2	+	diffuse	intact	
21	F	50	forehead	25 mm.	3 years	1	++	local	intact	Pigment noted clinically
22	M	—	neck	8 mm.	6 years	1	+++	diffuse	ulcerated	Pigment noted clinically
23	M	49	back	—	16 years	1	+++	diffuse	—	Pigment noted clinically
24	F	35	face	5 mm.	5 years	1	+++	local	intact	A mole clinically. Diagnosed histologically as melanoma with malignant change; no recurrence after 6 years
25	M	67	eyelid	6 mm.	4 years	1	+	local	intact	
26	F	53	neck	4 mm.	6/12	3	++	diffuse	intact	
27	M	45	scalp	13 mm.	years	3	+++	diffuse	intact	
28	F	55	eyelid	4 mm.	2 years	3	++	diffuse	intact	
29	M	70	cheek	17 mm.	2 years	3	+	diffuse	ulcerated	
30	F	—	cheek	10 mm.	—	1	++	diffuse	ulcerated	
31	M	60	face	14 mm.	5 years	5	++	diffuse	intact	
32	F	68	face	13 mm.	10 years	1	+	diffuse	intact	
33	M	65	—	16 mm.	—	2	+++	diffuse	ulcerated	

TABLE 1

No.	Sex	Age	Site	Size	Duration	Histological Type	Amount of Pigment Histologically	Pigment Distribution	State of Epithelium	Comment
1	F	58	chin	14 mm.	—	1	++	local	ulcerated	
2	F	52	leg	30 mm.	years	6	++	diffuse	ulcerated	
3	M	64	temple	3 mm.	years	1	++	local	—	Pigment noted clinically
4	M	81	cheek	4 mm.	1 year	3	++	local	ulcerated	
5	M	59	temple	4 mm.	1 year	3	++	diffuse	intact	Marked pigment present clinically
6	M	84	cheek	8 mm.	4 years	3	++	diffuse	ulcerated	
7	F	70	abdomen	13 mm.	7 years	1	++	diffuse	ulcerated	Pigment noted. One other tumour present non-pigmented clinically
8	M	48	chest	12 mm.	life	1	++	diffuse	ulcerated	Fungating mole clinically
9	F	59	forehead	10 mm.	years	3	+	local	ulcerated	
10	F	78	forehead	20 mm.	—	2	+++	diffuse	intact	
11	F	68	thigh	17 mm.	8 years	1	+++	local	intact	Melanoma clinically
12	M	49	face	16 mm.	—	5	+	local	intact	
13	M	—	forearm	8 mm.	15 years	1	++	diffuse	ulcerated	
14	M	51	face	5 mm.	—	1	+	local	intact	
15	F	43	nose	9 mm.	10 years	3	++	diffuse	ulcerated	
16	F	59	back	36mm.	years	1	+	diffuse	ulcerated	Multiple melanomata clinically
17	F	72	ear	15 mm.	8 years	2	+++	diffuse	intact	Pigment noted. Histologically diagnosed as melanoma
18	M	62	nose	6 mm.	—	1	++	diffuse	intact	Melanoma clinically. Histologically diagnosed as malignant melanoma
19	M	56	eyelid	2 mm.	6/12	1	++	diffuse	intact	Melanoma clinically. Histologically diagnosed as malignant melanoma
20	M	55	back	11 mm.	—	2	+	local	ulcerated	Multiple basal cell tumours clinically
21	M	65	neck	16 mm.	20 years	1	++	diffuse	intact	Pigment noted—tumour in old scar
22	M	27	scalp	13 mm.	—	1	+++	diffuse	intact	
23	M	77	cheek	5 mm.	2 years	1	+	local	intact	
24	—	—	eyelid	3 mm.	—	2	+++	diffuse	intact	
25	M	68	chest	12 mm.	20 years	3	+	diffuse	ulcerated	Multiple tumours. Pigment noted in one
26	M	40	neck	9 mm.	—	3	++	local	ulcerated	Pigment noted clinically
27	M	58	forehead	3 mm.	3 years	4	++	diffuse	ulcerated	
28	M	30	nose	6 mm.	4 years	3	+	diffuse	ulcerated	Pigment noted clinically
29	F	50	neck	12 mm.	5 years	3	+++	diffuse	intact	Pigment noted clinically
30	M	66	cheek	11 mm.	4/12	3	+	local	ulcerated	Pigment noted clinically
31	M	59	nose	5 mm.	4/12	1	+	local	intact	Pigment noted clinically
32	M	63	temple	12 mm.	14/12	2	+++	local	intact	Pigment noted clinically
33	M	?	leg	12 mm.	years	4	+	diffuse	ulcerated	

TABLE 2

Age incidence of pigmented basal-cell tumours.

Age	No. of Cases
20-30	1
30-40	3
40-50	8
50-60	22
60-70	13
70-80	9
80-90	2

TABLE 3

Table showing the sites of the tumours correlated with the amount of pigment present histologically.

Site	Total No.	Amount of Pigment		
		+	++	+++
Temple	4	1	3	—
Forehead ..	5	1	4	—
Eyelid	5	2	2	1
Ear	1	—	—	1
Cheek	10	6	4	—
Nose	11	8	3	—
Chin	2	1	1	—
Neck	6	—	4	2
Scalp	3	1	—	2
"Face"	6	2	2	2
Chest	2	1	1	—
Back	4	3	—	1
Buttock ..	1	—	1	—
Arm	1	—	1	—
Thigh	1	—	1	—
Abdominal wall	1	—	1	—
Leg	2	1	1	—
Unclassified ..	1	—	—	1

TABLE 4

Table showing the incidence of the histological types and correlating them with the amount of pigment present histologically.

Types	Nos.	Amount of Pigment		
		+	++	+++
1	25	9	11	5
2	9	3	—	6
3	22	10	10	2
4	6	3	3	—
5	3	1	2	—
6	1	—	1	—

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MALIGNANT SYNOVIOMA

WITH SPECIAL REFERENCE TO DIVERSITY OF TISSUE DIFFERENTIATION

By G. G. HARKNESS

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THE malignant synovial tumours are not common but are important surgically because, at operation, the tumour has a benign appearance. This is misleading because generally it exhibits a high degree of malignancy with both local recurrences and distant metastases.

In a recent article King (1952) records a series of 21 cases; of these, 11 had died with metastases within three years (9 showing pulmonary metastases), 3 were still well after five years, and 5 were known to have a recurrence or metastasis, but were still alive. The fate of the remaining 2 was uncertain.

Of the 2 cases reported herein, one died with widespread metastases within nine months, but it is too soon to know the outcome of the second case.

Histologically, the tumours, as will be shown, are of special interest in that they exhibit an unusual degree of tissue differentiation. This variability of the histological structure has led to some confusion, both in our understanding and naming of the tumours.

HISTORICAL

In the early reports, the histological features apparently were not appreciated, and the growths were considered to be spindle-cell sarcomata which occurred in relation to a joint. Lejars and Rubens-Duval in 1910 described a series of cases in which they noted, in the sections, the presence of spaces or clefts with a cellular lining and they considered the tumours to be endotheliomata. It should be noted that at this period the synovial lining was also considered to be a separate and distinct endothelium.

In 1927 Smith recognized that these tumours constituted a special group and he applied the name synovioma to them. He appreciated that there were histological differences between these and other connective tissue tumours. He also realized that the tumours may occur outside the actual joint space, and he classified them into articular, bursal and fascial types.

King, in 1931, in a study of tumours of this kind occurring in relation to tendon sheaths, made an advance in our concept of synoviomata, in that the tissue spaces found in these tumours were an example of a special type of tissue differentiation; the essential similarity of this type of tissue to synovial tissue was emphasized.

In 1938, Berger pointed to the presence of areas of mucoid change which occurred in some of these tumours and he considered that both this feature and the formation of synovial spaces were examples of tissue differentiation in the neoplastic tissue.

In 1942, Fisher, in a review of 42 cases, considered that the definite cellular lining of the tissue spaces warranted, as a name for the group, the term sarcomesothelioma. Fisher drew attention also to the occurrence of tumours histologically of the same pattern, but occurring in the limbs outside joints and not in relation to bursae or tendon sheaths.

More recently, Bennett (1947) reviewed a series of 32 cases which had been registered with the American Army Institute of Pathology during the period 1941-45. He clearly appreciates the nature of the tumours and describes three types of tissue differentiation, namely:

(i) tissue spaces which vary from clefts to well defined gland-like spaces containing serous or mucinous fluid;

(ii) tufts of cells varying from compact groups of oval or polygonal cells segregated in solid portions of the tumour to papillary projections extending into the tissue spaces;

(iii) masses of epithelium-like cells.

The most recent work on this subject is that of King (1952) who, in a review of 21 cases, clearly shows the various types of tissue differentiation which may be exhibited by the malignant synoviomata.

He describes four main types of tissue differentiation, from the basic spindle-cell tissue as follows:

(i) mucoid tissue of either cellular or cystic form;

(ii) spaces with a lining similar to synovium;

(iii) endothelium-lined spaces and "gland-spaces" with a lining similar to epithelium;

(iv) spheroidal epithelium-like cell tissues either in

(a) small groups of cells,

(b) epithelium-like strands — suggestive of the scirrhous carcinoma of the breast.

(c) cell masses of spheroidal cells distinct from each other and clearly demarcated from the surrounding tissue.

In any one tumour of this nature one form or another of these variations of tissue differentiation may be dominant to the exclusion of the remainder, and this has led to their being described as different types of synovial tumour.

The above brief historical review is by no means complete, but it is only intended to illustrate the phases in the development of the present concept of these tumours. The opinions of Bennett (1947) and King (1952) that the apparently differing histological pictures of these tumours are simply due to multi-differentiation, and that the growths constitute a single entity, are supported by the following case reports.

The first of these cases is recorded in some detail because in this tumour, and in fact in one section of it, all the various forms of tissue differentiation may be found.

CASE REPORTS

Case 1.

A female, aged 39 years, complained of pain in the right knee joint. She had had occasional twinges of pain in this knee for some years; six months previously she fell and injured the joint, and since then the pain had been continuous. Two days before being seen she fell and hurt the knee again. The pain had always been on the inner side.

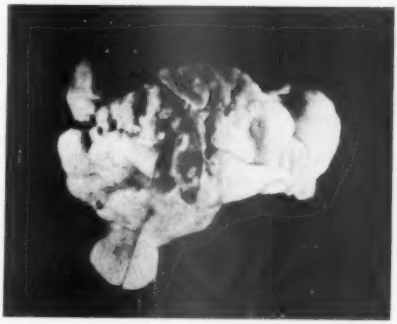

FIG. I. Photograph of the tumour (Case 1). It is lobulated, firm and cream in colour and with a smooth surface. Natural size.

On examination, the knee joint contained excess fluid and there was slight wasting of the quadriceps. The joint moved well considering the amount of fluid present. On the medial side of the knee above the joint line and at the level of attachment of the tibial collateral ligament there was a squashy tender swelling about 2 cm. in diameter; it felt cystic. McMurray's sign and other meniscus signs were negative. X-ray examination showed a small ? osteophyte at about the site of the swelling, but otherwise the film was negative.

FIG. II. Low power photomicrograph of a section of the tumour (Case 1) showing the varied tissue pattern. (x 4.)

FIG. III. High power photomicrograph of portion of a cellular area of the tumour (Case 1) showing spindle-cells with "active" nuclei. (x 480.)

Pre-operative diagnosis was ? Cystic medial meniscus ? Synovioma.

At operation, the joint was opened through the medial triangle. A lobulated, white, firm mass presented and a thick stalk led back to a site deep to the medial collateral ligament. This stalk looked less innocent than the main body of the tumour because it was streaked with blood vessels and had a fleshy appearance. Most of the medial meniscus was removed in order to provide adequate exposure. The incision was carried round below the line of the joint and the joint was opened behind the ligament. The stalk of the mass appeared to arise from a narrow base in the upper synovial recess deep to the ligament. The synovial membrane was dissected away from the bone and the deep aspect of the ligament. The removal of the stalk was macroscopically complete.

The tumour was considered to be a synovioma.

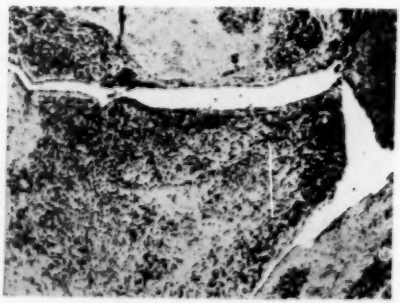

FIG. IV. Photomicrograph of part of the section of the tumour (Case 1) showing a synovial cleft and spindle-cell tissue. (x 36.)

Macroscopic Appearance.

The tumour was lobulated but roughly pear-shaped in general outline and measured 4.5 cm. x 4 cm. in its longest axis (Fig. I). It was cream coloured and of firm consistency. The cut surface was mucinous to both visual and tactile senses.

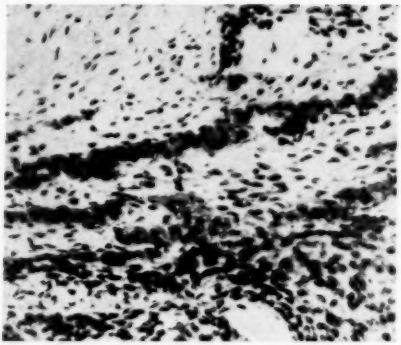

FIG. V. Photomicrograph of a portion of the section of the tumour in Case 1 showing two distinct types of differentiation. In the upper right corner of the illustration there is an area of mucin formation. The main portion of the photomicrograph shows cords and groups of spheroidal cells. This appearance is suggestive of that seen in a spheroidal cell scirrhous type of carcinoma of the breast. (x 125.)

Microscopic appearance.

There was a surprising variation in tissue patterns (Fig. II) and it is described here under headings of the most distinct types of pattern shown.

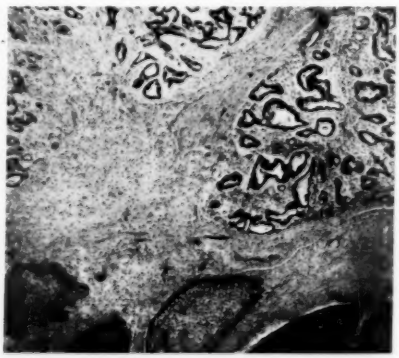

FIG. VI. Low power photomicrograph of another part of the section of Case 1 showing solid masses of spheroidal cells. In the upper part of the photomicrograph the glandular spaces are prominent. This is a higher magnification of upper middle area seen in Fig. II. (x 25.)

Spindle-cells and synovial spaces.

The predominant tissue was a spindle-cell connective tissue of varying degrees of cellularity. Quite large areas showed relatively few nuclei and heavy collagen formation with zones of hyaline degeneration, whilst other areas are exceedingly cellular with considerable nuclear variation, mitotic

figures and occasional multi-nucleated cells (Fig. III). In this tissue also clefts and spaces of the type seen in Fig. IV are common. These spaces frequently possess a cellular lining of flattened cells of the type usually seen in the synovial membrane.

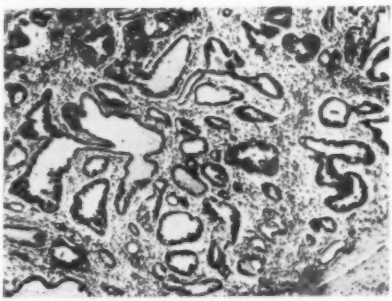

FIG. VII. Photomicrograph of the glandular portion of the section of the tumour shown in Fig. VI. This appearance is suggestive of an adenocarcinoma. (x 36.)

Mucoid changes.

In some areas the cells were more spheroidal and had a plentiful cytoplasm in which vacuoles were present; some appeared to coalesce to form areas of mucin (Fig. V upper right corner of illustration).

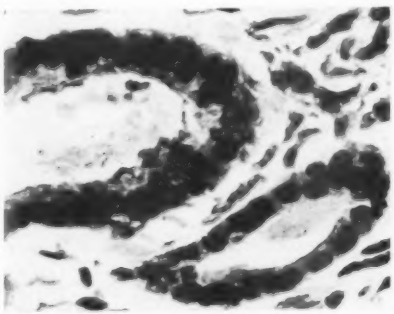

FIG. VIII. High power photomicrograph of the glandular spaces shown in Fig. VII. (x 480.)

Spheroidal cell tissue.

In the same area as the above, spheroidal cells with an abundant cytoplasm and an ovoid to round nucleus, are found, with the cells occurring in small groups and cords. The appearance is quite suggestive of that seen in a spheroidal cell scirrhous type of carcinoma of the breast (Fig. V). Adjacent areas consisted of large solid masses of spheroidal cells sharply demarcated from the surrounding tissues (Lower part Fig. VI).

Glandular and Endothelium-lined spaces.

In the same field of Fig. VI a very obvious glandular pattern can be seen. This is also illustrated under higher magnification in Fig. VII.

Under higher magnification again, these glandular spaces possess a cellular lining of endothelial type with the axis of the cell nuclei parallel to the surface. Or, as is more commonly the case, the cellular lining was epithelium-like, and here the nuclear axis was at right angles to the surface, and in some areas the cells appeared distinct from each other and were morphologically indistinguishable from a true epithelium. This can be well seen in Fig. IX.

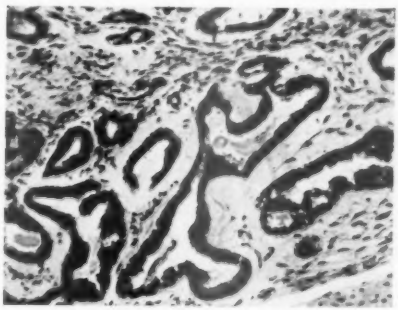

FIG. IX. Photomicrograph of the same glandular area of the section of tumour shown in Fig. VII. In this, and in Fig. VIII, the epithelium-like lining of the spaces is apparent. (x 100.)

Case 2.

A female, aged 19, complaining of three months history of injury to the left ankle, noticed a small lump on the sole of the left foot, not painful at first, but later she complained of burning pain in the lump and numbness across the ball of the foot. On examination, the left foot showed a small, hard, ill-defined mass lying beneath the plantar fascia.

At operation: Exploration of the sole of the foot showed a white, firm tumour below the plantar aponeurosis within the *flexor digitorum brevis* muscle and replacing the muscle fibres. The proximal limit of the tumour was not displayed. Laterally, the margin of the tumour corresponded with the lateral margin of the muscle limit of the lateral septum; the medial border was not dissected. A small portion of the tumour was removed for section. It appeared to be soft, pale yellow in colour and in one portion, gelatinous. An operative diagnosis of sarcoma was made.

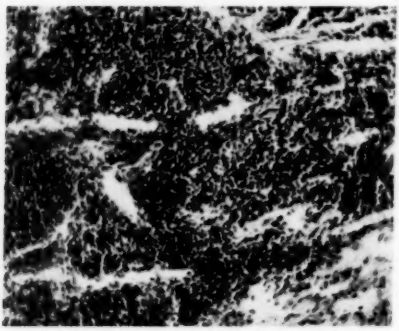

FIG. X. Photomicrograph of a section of the tumour from Case 2. Showing cellular appearance, spheroidal cells predominating. (x 100.)

Biopsy Specimen.

Macroscopically: the material consisted of two pieces of soft pale tissue measuring approximately 2 cm. x 1.5 cm. One end of one piece appeared to consist of muscle.

Microscopically: the tumour tissue appeared to infiltrate and destroy the muscle tissue but did not appear to arise from it. It was a cellular tumour, the cells being spindle and spheroidal in form, occurring in diffuse masses or in small clumps (Figs. X and XI). Typical synovial clefts and spaces were quite common (Fig. XI). The tumour was diagnosed as a malignant synovioma.

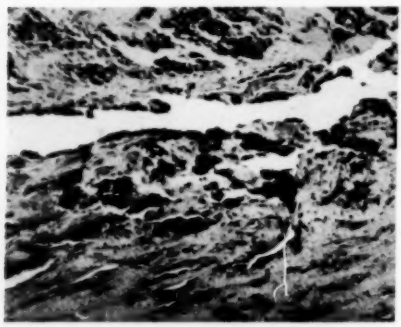

FIG. XI. Photomicrograph of another portion of the section of the tumour from Case 2. Showing a typical synovial space. There are groups of spheroidal cells in adjacent tissues. (x 100.)

The patient was treated by deep X-ray therapy. She developed a mass in the left supraclavicular region approximately seven months after the original diagnosis, but remained in fairly good health until she died in her sleep nine months after diagnosis.

Post-mortem showed metastases in the ovari-, kidneys, para-vertebral nodes, and in the hea-. This deposit, about 2 cm. in diameter, was situat- at the base of the inter-ventricular septum and w- considered to have caused interference with t- conduction system and responsible for the sudd- and fatal cardiac failure.

Histologically, the metastatic deposits appear- as an undifferentiated sarcoma (Fig. XII).

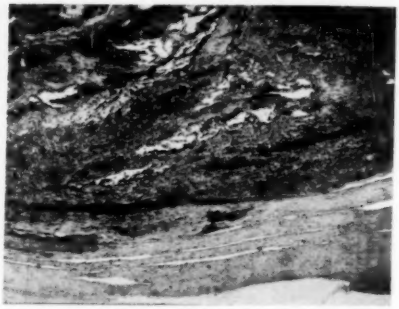

FIG. XII. Photomicrograph of a section of the metastatic deposit in the heart (Case 2). (x 35.)

DISCUSSION

The synovial tissue arises in the foetus from mesenchyme. This undifferentiated connective tissue in the vicinity of joints under the influence of ill-understood "organizing influences" forms a solid but loose-textured mass around the cartilaginous bone ends. Then a cleft containing tissue fluid forms at this point; this is the joint cavity. On its outer surface the connective tissue differentiates to form the joint capsule. On its inner surface the synovium differentiates from this primitive connective tissue. However, the ability of connective tissue elsewhere to form a synovium is not lost after foetal life as can be seen by the development of a synovium in a "false joint" or the synovial lining which forms in adventitious bursae.

Histologically, the normal synovial layer consists of a loose connective tissue composed of spindle-cells, fibroblasts, elastic fibres, and fat cells either singly or in groups. At its inner surface the connective tissue differentiates into a lining layer which, however, has not a complete cellular lining. But in many circumstances, particularly in irritative conditions it has a definite lining consisting of cells of varying appearance from flattened cells with sparse nuclei to

many layers of low cuboidal cells. This is the synovial membrane. It contains macrophage cells and in certain areas it is able to secrete mucinoid material (Kling, 1931).

In inflammatory conditions this synovial epithelium may become luxuriant and show large tufts and groups of spheroidal type cells.

King (1932), in his study of the "Pathology of Ganglion," shows the stages of the formation of a ganglion.

The earliest stage is an aggregation of the connective tissue spindle-cells in which spheroidal cells appear. In the cytoplasm of some of the spheroidal cells, mucin-containing vacuoles appear and these coalesce to form mucin filled cystic spaces, which develop a synovial lining.

From these facets of development, histology and inflammatory response of the normal and non-neoplastic synovial tissue, I have attempted to show that the basic spindle-cells of the synovium have the capacity to and do show differentiation into:

(1) spindle-cell tissue;

(2) synovial membrane which may show groups or tufts of cuboidal epithelium-like cells;

(3) spheroidal cells and from these areas of mucin may form;

(4) mucus-containing cysts which form a synovial lining.

This capacity of tissue differentiation exists in the normal synovial tissue and this same capacity of diverse tissue differentiation is shown by this group of malignant connective tissue neoplasms—the malignant synoviomata.

SUMMARY

Two cases of malignant synovioma, one of which shows an unusual diversity of tissue differentiation, are recorded. The histological nature of the tumours and the conclusion that the malignant synoviomata are connective tissue neoplasms which possess the same capacity of diverse tissue differentiation as is shown by the normal connective tissue of the synovium is discussed.

ACKNOWLEDGEMENTS

I wish to thank Dr. E. Abrahams, Queen Victoria Hospital, Melbourne, for material from the second case, and Dr. R. Motteram, Austin Hospital, Melbourne, for the post-mortem findings.

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Es aller fürtreff-
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sten gschöpffs aller Creaturen / von Got
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factur / aller eusserlicher vnd innerlicher glider vnnd gliedstuck / auß
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Allen denen so die herrlichen vnergründtlichen wunderwerck Got-
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sprach verfasset vnd an tag geben. Normals weder
gesehen noch gelesen worden.

Durch M. Gualtherum Hermenium Ryff /
Argentinum / Medicum.

Rumpt her / vnd schawet die werck des Herren / dann der Herr ist
wunderbar / vnd seine werck vnergründtlich.

M. D. XLI.

Mit Königklicher Mate. Freiheyt.

FIG. I The title page of the 1541 edition of Ryff's book on Anatomy.

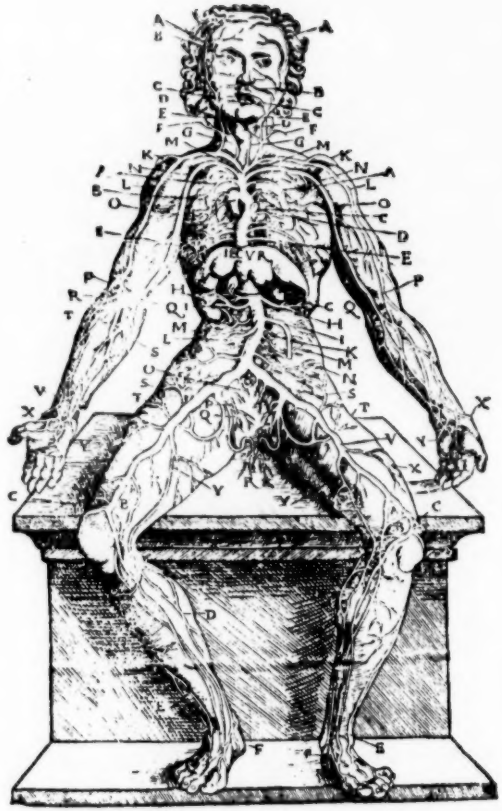

FIG. II. The illustration of the venous system copied from the second table of Vesalius but superimposed upon a seated figure.

The College Library

WALTER HERMANN RYFF AND HIS ANATOMY

By K. F. Russell

Department of Anatomy, University of Melbourne

WHEN Andreas Vesalius prepared his *Tabulae Sex* and issued it in Venice in April, 1538, he little suspected that it was to become the subject of almost immediate plagiarism by authors all over Europe. The six tables were, of course, by far the best picturization of the anatomy of the skeleton, vessels and viscera that had appeared up to that date and, as such, were quickly seized upon by authors for their own use. This was in spite of a licence of copyright given to Vesalius and printed at the foot of the last Table.

Vesalius was excceedingly annoyed at the many plagiarisms committed against him and a few years later, in a letter to Oporinus on the printing of his *Fabrica*, expressed himself quite forcibly on the subject:—

> "But these privileges are often not worth the paper they cover, as I know but too well, from what happened to my Anatomical Tables published at Venice three years ago, the value of decrees of sovereigns issued to printers and booksellers who swarm everywhere and have marred my works in putting them forth under pompous titles."

Later, in the same letter, he goes on to say:—

> "Worst of all, so far as science is concerned, at Strassburg, another plagiarist, whom Fuchs greatly blamed, thought fit to contract the size of the plates, which can hardly be too large, to daub them with ugly colouring, and to surround them with a text borrowed from that of the Augsburg edition, but put forth as his own." (Cushing: *Bio-Bibliography of Andreas Vesalius.*)

The Strassburg plagiarist was Walter Hermann Ryff and the College Library has a splendid copy of his *Anatomi* which was published in 1541.

Ryff published a large number of books on subjects as diverse as the art of cooking, obstetrics, surgery, hygiene, pharmacy, mathematics and architecture as well as the one on anatomy, but very little is known of his life. He was born in Strassburg, and lived in Mainz prior to 1539, he then moved to Nürnberg where he was physician to the city between 1549 and 1551. He died some time prior to 1562 which was the year of publication of his *Grosse Chirurgia* (Gurlt, 1898).

Ryff, to say the least, was an opportunist and when he saw the *Tabulae Sex* he must have got to work at once on his anatomical book. Not content with direct borrowing of the Vesalian plates he also used the illustrations of a number of other authors. There are a number of small woodcuts of the foetus *in utero* taken from Eucharius Rösslin's *Der swangern Frawen und hebammen Roszgarten*, 1513; there are nine large woodcuts of the brain and skull taken from Johann Dryander's *Anatomia capitis humani*, Marpurg, 1536; one of the tongue and palate and two woodcuts of the superficial muscles of the body are taken from another of Dryander's books; the woodcut of the eye and optic nerve is taken from Gregorius Reisch's *Margharita philosophica*, Basle, 1504; the seated figures of a male and a female showing visceral anatomy owe much to Lorenz Fries's *Spiegel der Artzny*, Strassburg, 1518, and were in turn copied from Ryff by Loys Vasse in the 1553 edition of his *In Anatomen corporis humani tabulae quatuor.* Ryff altered the pose of the Fries figures and seated them on a rather ornate bench.

FIG. 1 The title page of the [illegible] Ryff's book on Anatomy.

copied from the second table of Vesalius' [illegible] superimposed upon a seated figure.

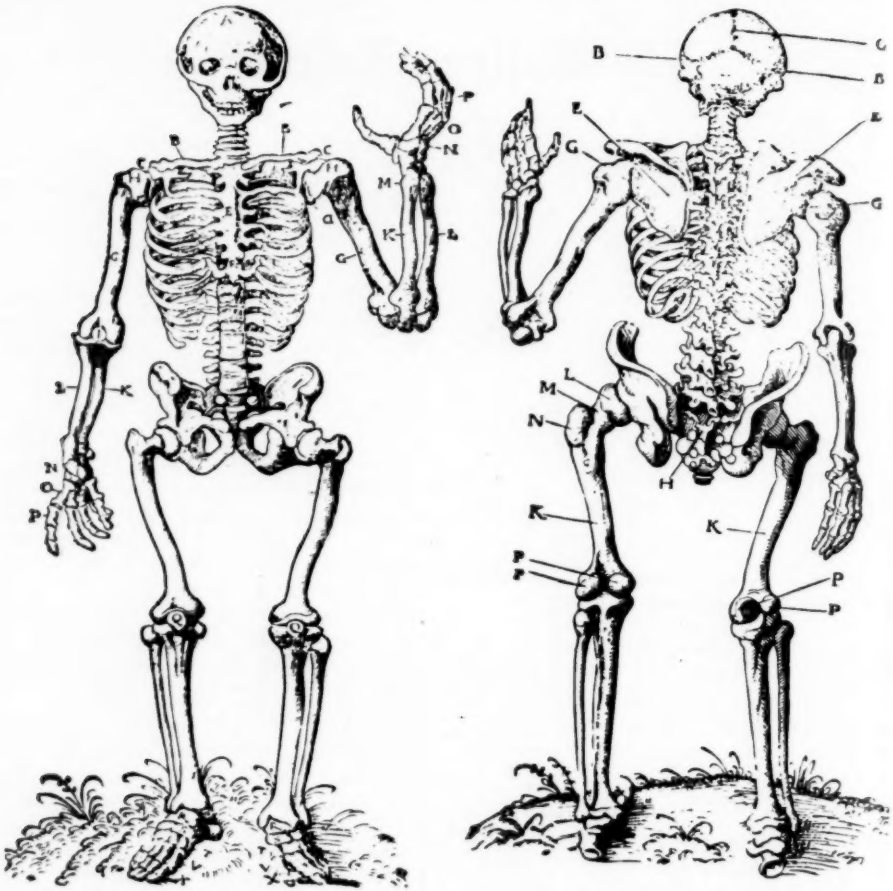

FIG. III. Anterior and posterior views of the skeleton as reproduced by Ryff.

It is interesting to note how Ryff treated the Vesalian plates. So far as the figures of the arteries and veins are concerned, Ryff was shrewd enough to superimpose the Vesalian woodcuts upon the seated outlines of male and female figures. This was, in fact, a marked improvement on the original for it showed the relationship of the vessels to the trunk and limbs in a much better way than Vesalius who had only produced schematic drawings. In some copies the vessels have been coloured with good results (Cushing, 1943). Ryff retained the same lettering of the vessels that was used by Vesalius.

In the case of the three views of the skeleton, Ryff made some alterations. At best they are very poor copies of the originals, the proportions of the skeleton have been altered resulting in ugly, stunted figures as can be seen in the illustration: the figures were also reversed but the same lettering was used. Ryff's artist had little or no knowledge of osteology for, when he copied the figures, he gave the skeletons only ten complete ribs and ten thoracic vertebrae. The curious anomaly of almost complete absence of the first rib is certainly due to lack of knowledge as is the fact that the second rib appears to articulate with

the scapula. In the lateral view of the skeleton there is a very peculiar acromioclavicular articulation and the anterior and posterior views of the left shoulder joint are very ill drawn. The epiphyseal lines were copied from the Vesalian plates. There is, however, a correction made by Ryff to the illustration of the anterior view of the skeleton. In the Vesalian figure the sternum is composed of seven pieces, a relic of the anatomy of Galen; in the Ryff figure the sternum is in one piece. His correction may or may not have been deliberate; in view, however, of the artist's poor attempt to copy the Vesalian figures it is more likely that the correction is attributable to bad copying rather than to anatomical knowledge.

It now remains to consider Ryff's own remarks in his book on the question of authorship. In the verbose and pompous title he states that he has edited the work in the German language for the first time; the inference being that he has collected the work from other languages and translated it into German. However, the next sentence states that the work "has not been seen or read before." In his preface there is a more direct reference to his authorship for he says:—

> " . . . I have been induced to describe diligently and in an orderly German language such a creature, so that everybody could easily recognize himself in it and could view himself, as in a clear, pure mirror."

His book was composed primarily for the lay public and this fact is indicated by the naïve exhortation on the title:—

> "Come along and look at the Work of the Master, for the Master is wonderful and his Work unfathomable."

There can be no doubt but that Ryff was a very successful plagiarist and that he issued his book as his own. He was even careful to obtain a Royal copyright for his book and bold enough to have his privilege printed on the title. But it must be remembered that Ryff was no better or worse than many other authors of the period when plagiarism was commonplace. In point of fact he may even have paid Vesalius an indirect compliment by enabling more people to see his work and read it in their own language.

It is interesting to note that Haller in his magnificent *Bibliotheca Anatomica* has entirely overlooked the fact that Ryff copied the Vesalian plates for he says of the book:— *Icones Dryandri repetit, tum conjunctas. tum inter sermonem anatomicum & physiologicum interspersas.*

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CHRONIC SCLEROSING PERI-SYNOVITIS OF THE DORSUM OF THE HAND

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THE degree of disability which may follow an apparently minor injury to the hand is well known. Frequently trauma, which would not be described as severe, is followed by a long period of incapacity, and in some cases by enough permanent impairment of function to make a change of occupation necessary. For example, a finger injury resulting in laceration of the pulp, fracture of a phalanx or sprain of a joint, may cause the loss of weeks or months of working time and result in permanent loss of function.

Less commonly recognized as a cause of disability are the conditions which may be produced by an injury to the back of the hand. It is proposed to discuss a special group of these conditions, as illustrated by three cases in which a comparatively slight injury to the dorsum has resulted in several months of disability. In two of them permanent impairment of function seems probable. A fourth case is added because of the similarity in pathology, although disability in this case has been minimal.

Case Reports

Case 1.

T.M., a motor mechanic, aged 25 years, was seen in October, 1949. He stated that nine weeks previously he had struck the back of his left hand with a spanner. A swelling appeared during the next two hours and he consulted his doctor who arranged an X-ray. This showed no fracture.

Over the next two weeks the swelling gradually subsided but did not disappear completely and when he resumed work there was still a lump on the back of his hand. He found that, with use of the hand, this became painful and at the end of the day there was a much larger swelling which he could indent with his finger. Overnight this swelling would subside but the smaller hard lump remained.

On examination there was a firm oval swelling with indefinite edges one and a half inches in diameter on the dorsum of the left hand. The skin could be moved over it but the swelling could not be moved on the deeper structures. Movement of the fingers was normal and did not affect the swelling. There was no pitting oedema at this time.

On 28th November, 1949, under general anaesthesia and with haemostasis determined by a pneumatic tourniquet, the swelling was exposed. It consisted of a plaque of dense fibrous tissue surrounding the tendons of *extensor digitorum communis* just distal to the retinaculum and infiltrating the tendons in such a way that it could be removed only by sharp dissection. The hand was bandaged to a plaster splint for eight days. Active movements were then begun and restoration of normal function was rapid.

He returned to work early in January, 1950, five months after his injury, and when last seen on 23rd January the hand appeared normal. He was working without any disability.

A recent report (April, 1952) is to the effect that he has had no further trouble.

Unfortunately no histological examination of the excised material was made in this case.

Case 2.

C.K., a timber worker, aged 33 years, was lifting a heavy piece of timber on 2nd October, 1950, when he felt a sudden pain in the back of the right wrist and forearm. He states that his right middle and ring fingers were "paralyzed" and he was unable to straighten them. This patient had previously ruptured some of the extensor tendons in the lower forearm in a similar accident in 1946 and they had been sutured. His doctor feared that the same thing had happened again and therefore on 5th October explored the site of the previous rupture. There was no rupture of the tendons, nor any other significant abnormality. His hand and forearm were placed on a plaster splint for two weeks. Within a few days of the operation it was noted that the back of the right hand was very swollen. The swelling persisted after the splint was removed and the patient stated that the back of the hand "felt very hard." After a course of physiotherapy he was still unable to use his hand to any extent as movement was painful and the swelling was still present. He continued to have

physiotherapy, alternating with periods of immobilization in plaster, for three months.

When the patient was seen on 7th February, 1951, there was a diffuse firm swelling over the dorsum of the hand. It did not pit on pressure. The patient had noticed, however, that when he had attempted to use the hand the swelling had increased and on these occasions pressure on it with the finger "made a mark." Extension of the fingers was full but there was considerable limitation of flexion—he could not "make a fist." Thumb movement was normal. There was no evidence of bone injury in an X-ray.

He was advised to discard his splint and to try using the hand again.

He was seen, at this stage, by Mr. A. J. W. Ahern who suggested the possibility of a diffuse fibrosis of the dorsum of the hand and advised exploration.

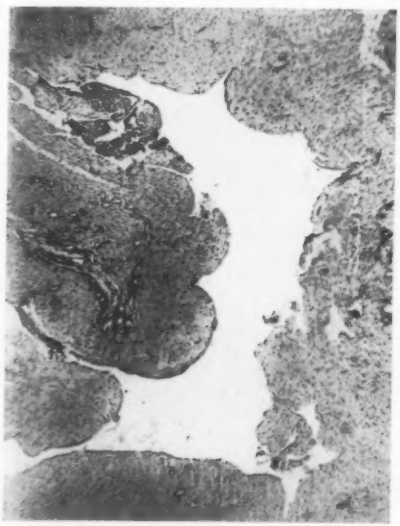

FIG. I. Photomicrograph of section of material excised in Case 2, showing fibrous tissue with a synovial space. (x 30.)

This was carried out on 21st February and showed a mat of dense fibrous tissue covering the entire dorsum. It extended far beyond the tendons and their sheaths. The tendons were identified by tracing them distally from under the retinaculum where they disappeared into the fibrous mass. They were freed by sharp dissection and the fibrous tissue was removed. The hand and forearm were immobilized by plaster for seven days and then movements were begun.

By 24th March, movement of the fingers was of normal range. There was a slight swelling on the dorsum of the hand but the patient returned to work.

He reported on 27th April that he was doing heavy work as a sleeper cutter and having no trouble with his hand.

On 16th June he attended with a pain in his right wrist brought on by another injury. The dorsum of the hand was normal. He was treated for a sprain and he returned to work on 9th July.

On 8th August, he reported that he had injured the back of his right hand again on 16th July. The hand had become swollen immediately afterwards and had not subsided. Examination showed pitting oedema of the dorsum. Finger movement was normal.

He was advised to find work in which he was less liable to injury. His doctor reports that he has done so, and is not having much trouble with the hand. There is, however, some induration to be felt over the dorsum, and excessive use causes some pitting oedema.

Histological examination of the excised tissue shows a moderately cellular fibrous tissue with groups of small round cells mainly in the vicinity of the blood vessels. There are several spaces to be seen, and these are lined by connective tissue of typical synovial appearance (Fig. I).

Case 3.

E.B., a timber worker, aged 44 years, was struck on the back of the right hand by a motor-saw blade, the teeth of which punctured the skin in three or four places. The hand became very swollen and at one stage there was some purulent discharge from one of the puncture wounds. He returned to work four weeks after his injury but found that use of the hand caused pain over the dorsum, and swelling which would subside with rest.

He was first seen on 10th July, 1951, nine weeks after the accident. There was an ill-defined, firm swelling about one inch in diameter on the dorsum of the hand just below the level of the wrist joint. X-ray examination showed no abnormality.

It was suspected that the swelling was a localized area of fibrosis but as there was some doubt about the severity of his symptoms he was advised to make another attempt at his usual work.

He reported again on 8th October, saying that he had been working at intervals but that any heavy work made the hand "puff up."

On 30th October, exploration was carried out. The firm swelling noted previously was indeed fibrous tissue but in addition to this localized mass there was a thinner layer of fibrous tissue over the entire dorsum, extending up under the retinaculum. The latter had to be divided in order to remove the

tissue which enveloped the extensor tendons completely. The dissection was carried down as far as the metacarpal heads and from one side of the hand to the other. Movements were begun after eight days.

The patient returned to the country on 21st November, 1951, at which time there was still some induration over the back of the hand.

He was seen again on 19th December when the hand appeared normal. However, he had been working as a pea-picker and said that by the end of the day the hand would be swollen in the same way as before the operation. He was advised to find other work for the time being and to wear an elastic bandage on the hand and forearm. He was shown how to apply the bandage.

He returned on 23rd February, 1952, with the bandage wound tightly around the wrist and oedema of the back of the hand. He admitted he had only applied the bandage that day, and had been picking peas in the previous four weeks. After removal of the bandage the oedema subsided and next day it was apparent that there was some induration on the dorsum of the hand. He went off to find other work and has not been seen since.

FIG. II. Photomicrograph of a section of tissue excised in Case 4, showing a synovial space containing a mass of fibrinous material (loose body) and surrounding fibrosis. (x 8.)

Case 4.

W.W., a farmer, aged 49 years, was seen on 25th February, 1952, when he complained of a swelling on his left hand for the previous five months. He could not recall any injury before the swelling appeared, but said he frequently knocked his hands. When the swelling first appeared it was the size of a pea. He was advised to "hit it with a book." Someone did this for him and for three days the hand was very painful. A week or so later he noticed that he had a second swelling adjacent to the original one which was still present. This new swelling was much larger than the first. Over the next four weeks he developed still another which appeared to be attached to the second one. The condition caused only slight discomfort and did not affect the use of the hand, but in view of the increasing size of the lesion he wished to have it removed.

There was a firm swelling two inches long and half an inch wide on the ulnar side of the dorsum of the hand. It was lobulated and three main parts could be distinguished, representing the three lumps he described. It could be moved from side to side, but not in a longitudinal direction. Finger and wrist movements were normal. It was regarded as a ganglion and arrangements were made for its removal.

FIG. III. Photomicrograph of section of the tissue (Case 4) showing synovial spaces and accumulation of wandering cells between there. (x 25.)

On 26th February, under general anaesthesia and with haemostatic control by a pneumatic tourniquet, the swelling was exposed. It consisted of fibrous tissue surrounding the tendon of *extensor digiti minimi*. It was far more extensive than was suspected from clinical examination and fibrous tissue was removed from above the retinaculum to a point just above the metacarpal head. In the course of dissection, fluid-containing spaces were opened and from these some loose bodies

escaped (See Fig. II). Movements were begun after five days and when seen on 15th March, function of the hand was normal. There was some thickening lateral to the upper end of the scar.

He was seen again on 17th April, when this thickening appeared to be less, but it was still present.

FIG. IV. Higher power photomicrograph of a synovial space (Case 4) showing the cellular character of the membrane and the accumulation of wandering cells around this. (x 75.)

Examination of a section of the material excised shows dense collagenous tissue with many collections of small round cells scattered through it. There are several spaces lined by cellular connective tissue of typical synovial types (Fig. III). The lining cells are irregularly spheroidal and spindle with a considerable amount of protoplasm and relatively large nuclei, and these are orientated at right angles to the surface of the space (Fig. IV).

CLINICAL FEATURES

Four patients with a swelling on the back of the hand have been described. In Cases 1 and 3 there had been a direct blow on the hand, in neither case heavy enough to cause a fracture. In Case 4 a swelling appeared without any known antecedent trauma, but increased greatly in size after a blow. Whether the original swelling was of the same pathological nature as the tissue which was excised cannot be known with certainty. In Case 2 there was no direct injury to the back of the hand, and the pain was referred to the wrist and lower forearm. The surgical procedure which followed was carried out on the lower forearm, so that if the subsequent swelling on the back of the hand is to be related to either the injury or the operation the most likely explanation is that extravasated blood spread to the hand from a higher level.

In Cases 1, 2 and 3, swelling was present within a short time of injury and was regarded as a haematoma and reactionary oedema which would subside in the course of a week or two. However, it failed to do so beyond a certain stage and a hard lump remained in the region. Case 4 followed a similar course up to this point, but subsequently had little pain and no increase in swelling with use of the hand. The others, however, felt pain in the region of the lump when the hand was used and developed a puffy swelling with excessive activity. Two of the patients had noticed that this swelling could be indented by pressure and there seems no reason to doubt that in all three cases the additional swelling brought on by heavy work was due to a pitting oedema.

The characters of the swelling were the same in all four cases. A firm mass, with indefinite edges and fixed to the deeper structures, occupied a part, or in one case almost the whole, of the back of the hand. Limitation of flexion of the fingers was present in one case but may have been due to prolonged immobilization. Three of the cases were examined by X-ray and showed no abnormality.

The duration of the symptoms should be noted. Case 1 had suffered his disability for four months and Case 2 for four and a half months before operation. Case 3 had been unfit for his ordinary work for six months. Case 4 had not been prevented from working but had been aware of the swelling for five months.

The clinical features may be summarized thus: A mild injury to the hand is followed by swelling which does not subside completely but leaves a firm, fixed mass on the dorsum. Pain is felt in this when the hand is used, and a pitting oedema may develop,

preventing the patient from doing manual work. The condition persists for months without any improvement.

THE NATURE OF THE LESION

The development of "hard oedema" of the dorsum of the hand after an injury was first described in 1901 by Secrétan. The subject is discussed at some length by Iselin (1940) who describes a mild injury followed by persistent painful "hard oedema" which does not pit on pressure. It is limited to the back of the hand and does not involve the wrist and fingers. In some cases it remains localized to one part of the dorsum. The clinical picture he presents is identical with that of the cases reported here and it could be assumed that the pathology present in this "hard oedema" was fibrosis around, and in some cases beyond the limits of, the extensor tendons. Watson-Jones (1946) writes of peri-tendinous fibrosis of the dorsum of the hand as being identical with the dorsal oedema of Secrétan (who also speaks of a traumatic hyperplasia) and describes the presence of "thickened hyperaemic fringes around the extensor tendons." Van Demark *et alii* (1948) report two cases similar to those described here in which they excised fibrous tissue from the back of the hand, and they identify the condition with that originally described by Secrétan and discussed by Iselin.

However, Iselin does not mention the actual tissue changes present and at no stage suggests that fibrosis plays any part in the condition. Leriche and Fontaine (1923) describe a "hard oedema" of the dorsum of the hand after injury which they regard as an actual oedema due to a vasomotor disturbance. Leriche has had good results from treatment by sympathectomy. Iselin refers to Leriche's views and it may well be that he is actually discussing this condition described by Leriche in which, in the early stages at least, there is only oedema, and no fibrosis. Other writers report cases of "hard oedema" of the hand but do not indicate whether they regard the condition as one of true oedema or as one of fibrosis. In the cases reported here the state of the tissues on the back of the hand has been seen and certain of the features may be discussed.

PATHOLOGY

The condition is one of fibrosis, macroscopically and microscopically. But it is also one in which differentiation to synovial tissue takes place, as is shown by the presence of synovial spaces. These can be demonstrated in pieces of tissue removed from parts of the dorsum remote from the normal synovial sheaths. In Case 1 the fibrosis did not extend much beyond the normal situation of the synovia but in the other three cases it was far more widespread. The condition is therefore not simply one of thickening of pre-existing synovial membranes. The condition may be likened to the formation of false bursae where injury results in fibrosis and the sliding movement of the tissues in the region determines differentiation and the formation of a synovial space.

Clearly these cases show the end result of whatever process is responsible, although Case 4 differs in the extreme degree of small round cell accumulation. In this case evidence of active inflammation suggests that the end of the process has not yet been reached.

It is apparent that the cases reported are of the same nature as those described by van Demark *et alii* (1948). These writers recognized the presence of fibrosis as the cause of the swelling of the hand but appear to have overlooked the synovial features.

If the "hard oedema" described by Iselin (1940), and by other writers quoted by him, is the same condition as that found here, they appear to have overlooked the fibrosis. This condition is a chronic inflammatory one and the result of quite a different process from that suggested as the cause of "hard oedema" by Leriche and Fontaine.

Pathogenesis

The condition is the result of some kind of injury to the tissues, usually a mechanical one. There is much to suggest that extravasation of blood is a factor but it cannot be the only one. In most cases a haematoma

resolves. It may, in certain circumstances, become organized and form fibrous tissue; in other circumstances it may form a cyst. There may be an associated circulatory disturbance, particularly in tissues subject to movement. Both organization and, in a sense, cyst formation have taken place in these cases, the cyst formation being represented by the synovial spaces. Circulatory changes were evident in three of the cases, with the development of oedema after use of the hand. They are not, however, an integral part of the process as observed in the present series of cases and this distinguishes the condition from that described by Leriche.

In the cases reported it is reasonable to assume the presence of extravasated blood after the injury. This appears to be the exciting factor in the development of the condition, but the other factors, which determine organization rather than absorption, are not known. The condition has been described as Chronic Sclerosing Peri-synovitis of the dorsum of the hand in an attempt to indicate the nature of a process in which chronic inflammatory changes progressing to fibrosis involve the peri-synovial tissues, sometimes only in their immediate vicinity and sometimes over a wide area.

PROGNOSIS

Because of doubt as to the exact pathology in the cases of "hard oedema" reported, it is difficult to apply the published views on prognosis to the condition under discussion. Watson-Jones (1946), however, regards "hard oedema" as being due to fibrosis and in his opinion the prognosis is poor. He states that recurrence is common after excision of the fibrous tissue.

In this group Case 1 appears to have been cured. Case 4 has no symptoms two months after the operation, and there is no recurrence of the swelling. Both these patients had localized lesions. Case 2 resumed heavy work and had no symptoms suggesting a recurrence of fibrosis for four months. At this time he sustained another injury and since then has had a swelling on the dorsum and oedema if he does heavy work. Case 3 had pitting oedema three and a half months after his operation and an area of induration on the dorsum. Thus, both the cases who had a generalized fibrosis show signs of a recurrence of the condition. They are able to use the hand but not for heavy work.

TREATMENT

Physiotherapy is likely to be ordered for a swelling of the hand which does not subside in the expected time. It was used only in Case 2 in this group and had no effect on the condition. It is unlikely to have much effect on dense fibrous tissue.

Watson-Jones (1946) advocates immobilization for many months in a plaster cast. Even after prolonged immobilization there may be no improvement.

Van Demark *et alii* (1948) suggests the early evacuation of a haematoma on the back of the hand in order to prevent the development of fibrosis. However, there is no certainty that a clinically recognizable haematoma will precede the fibrosis, and in any case most haematomata are absorbed without any sequelae, and their evacuation would be unnecessary.

Excision of the fibrous tissue has been followed by some evidence of recurrence in two cases of the four. They were the two cases in which the dissection was most extensive. In a subject in whom organization of a haematoma has occurred following an injury it is only to be expected that organization may occur in any extravasation of blood following excision. Therefore if excision is to be carried out, every attempt should be made to reduce the amount of extravasated blood present in the tissues after operation. This requires dissection without a tourniquet so that all severed vessels may be secured, and a pressure dressing.

In the localized lesions the result of excision has been satisfactory. In the cases of extensive fibrosis it has been less satisfactory but both patients say their hands have been improved. It is therefore considered that excision of the fibrous tissue, undertaken with due precautions to prevent further bleeding into the tissue, offers the best prospect of improving the function of the hand.

SUMMARY

1. Four cases of fibrosis of the dorsum of the hand are described.
2. The clinical feature of swelling occurring in the tendon sheaths and in the tissues beyond these, arising usually after an injury, is described.
3. The condition is one of a chronic inflammatory change following the injury; instead of simple resolution, which usually occurs, there is fibrosis and cystic (that is, synovial) development.
4. The prognosis is poor in that persistence or recurrence of the condition is often seen.
5. Excision of the sclerosed tissue is advocated in treatment.

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CASE REPORT

PERFORATION OF JEJUNAL DIVERTICULUM ASSOCIATED WITH ACUTE RETROGRADE JEJUNO-GASTRIC INTUSSUSCEPTION

By E. E. DUNLOP

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DIVERTICULA of the small intestine are not excessively rare in their incidence, though much less common than those of the large intestine. King (1950) reported an incidence of 0.6 per cent. in the subjects of post-mortem examinations in a general hospital for adults.

Surgical complications of such diverticula are, however, quite rare. Few cases of perforation of jejunal diverticula have been described. These include cases of traumatic rupture:—Butler (1937), Adams-Ray (1938), Schunk (1939). This variety results from violence to the abdomen, as in the classical example of a kick from a horse.

Due largely to the fact that jejunal diverticula, though thin walled, usually have a wide communication with the lumen of the intestine, spontaneous perforation is also quite rare. An extensive survey of the literature revealed references to cases suffering from this catastrophe by Treves (1900), Christie (1922), Spackman (1926), Fraser (1933), Flynn (1933), Butler (1933), Gerster (1938), Dodson (1941), Kozinn and Jennings (1941), Benson *et alii* (1943), and Walker (1945).

The following case is reported not only because of the rarity of spontaneous perforation of jejunal diverticula, but also because of the unusual circumstances that the perforation was associated with a retrograde intussusception of the jejunum through a gastro-enterostomy stoma, and thus occurred within the stomach.

CASE HISTORY

An engineer, aged 59 years, was re-admitted to the Royal Melbourne Hospital on 18th July, 1949. Sixteen years previously he had sought treatment for a stenosing duodenal ulcer of eight years standing. A retro-colic gastro-enterostomy was carried out by Sir Victor Hurley. The appendix was also removed. He enjoyed good health and worked actively for over fifteen years after this event. Towards the latter end of 1948 he experienced upper abdominal pain and vomited some "coffee grounds."

On New Year's Day, 1949, and thereafter for three days he experienced spasmodic central abdominal pain and repeated copious vomiting. On the following day his vomitus was described as "almost pure blood," and in alarm he sought admission to hospital.

By the time he was admitted to a medical ward, the symptoms had almost subsided. His blood pressure was noted to be 205/140 mm. of mercury, and his haemoglobin percentage was 104. It was thought on first examination that there was a small round mobile mass present to the right of, and below the umbilicus. His recovery was so rapid that investigations were deferred and he was discharged with an unconfirmed diagnosis of "? anastomotic ulcer with haematemesis and melaena."

On 18th July, 1949, he was again admitted to a medical ward with severe intermittent colicky epigastric pain and vomiting of altered blood. He stated that he had passed a dark motion on that morning. This vomiting continued and his condition deteriorated seriously. It was noted that the gastric content developed an extremely foul smell described as "faecal."

He was seen in consultation with Dr. K. D. Fairley on 22nd July, 1949. The foul smell of aspirated gastric content had led to consideration of the diagnosis of gastro-jejuno-colic fistula.

The abdomen was somewhat full and tense, and was held rather rigidly. There was a diffuse bulging of the epigastrium and an ill defined mass in this region was considered to be the stomach. Unavailing efforts were made to aspirate further fluid from this organ.

Some thought was given to the possibility of retrograde intussusception. No visible peristalsis was detected and peristaltic sounds did not appear to be excessive.

The arresting feature of foul "faecal" gastric aspirations led to further preoccupation with the diagnosis of gastro-jejuno-colic fistula. Operation was considered urgently necessary, and intravenous fluid replacement had already been thorough.

FIG. I. Photograph of the resected portion of the jejunum showing site of perforation.

Operative Findings.

A retrograde intussusception of jejunum to the stomach was found to involve about two feet of upper jejunum. Near the apex of the intussusception there was a ragged area of gangrene and perforation corresponding to the site of the jejunal diverticulum. This diverticulum was constituted by a broad bulge two inches across the base. It projected into the thickened mesentery but was centred somewhat to the right, and the perforation was largely on this aspect. The advancing foot of bowel was darkly congested and grossly oedematous, and there were devitalized areas. Though it was fairly certainly viable the friable state of the bowel wall, and the proximity of the perforation to the mesentery determined resection rather than closure of the opening. Accordingly, a foot of jejunum was resected and an end-to-end anastomosis effected.

FIG. II. Photograph showing the internal appearance of the resected loop with the site of perforation indicated by arrow.

Progress.

He made a very satisfactory recovery only marred by slight wound infection. He has remained well to this date.

COMMENT

Diagnosis.

The key points to the elusive diagnosis in this case were the known gastro-enterostomy, a rapid onset of colicky pain of the obstructive type, the vomiting of blood and the presence of an upper abdominal tumour.

The previous severe attack had subsided rapidly with complete disappearance of symptoms, suggestive of a mechanical event.

In extenuation it may be said that the writer has seen a case of gastro-jejuno-colic fistula in which super-added symptoms of intestinal obstruction were a marked feature. The gastric tumour appeared explicable on the basis of defective emptying of the foul fluid and debris which at times blocked the in-dwelling tube.

Adams (1935) reviewed from the literature 30 cases of retrograde jejuno-gastric intussusception subjected to operation, and reported one of his own. Of these, 9 died and 21 recovered. He counselled: "Where haematemesis or obstructive symptoms appear after gastro-enterostomy, think of intussusception."

The Perforated Jejunal Diverticulum.

The diverticulum may have played a purely passive role in this case. The thin wall constituted a vulnerable point where the "blow out" occurred. The bowel in the vicinity of diverticula frequently shows some general dilatation, and neuro-muscular inco-ordination and "atony" have been postulated as factors in their formation.

It is tempting to speculate as to whether chance alone determined the presence of a diverticulum at the apex of the intussusception, or alternatively, that this structure was associated with some disturbance of the uneasy peristaltic rhythm.

SUMMARY

1. A case of perforation of a jejunal diverticulum, complicating acute jejuno-gastric intussusception, is described.
2. The patient survived following operative resection of jejunum.
3. Both conditions are rare. The combination appears to be unique.

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Books Reviewed.

FRACTURES AND JOINT INJURIES. (Vol. I.)

By Sir REGINALD WATSON-JONES, B.Sc., M.Ch. Orth., F.R.C.S., F.R.A.C.S.(Hon.) Fourth Edition. Edinburgh: E. and S. Livingstone Ltd., 1952. 9¼" x 6½", xxiv plus 443 pp., 709 illustrations. Price: £6 per set of two volumes.

This new edition is beautifully produced and is a valuable contribution to the treatment of fractures. It has been awaited, not only by those who could not obtain copies of the earlier edition, but also by those looking for recent advances. And neither will be disappointed.

The matter in the first volume (the second will appear later) is absolutely up to date. For example, in the section on bone grafting the value of refrigerated homogenous bone is described. In many parts, the book is virtually a new one because so many sections have been altered or rewritten. In fact, it brings all the subjects dealt with right up to our knowledge at the present time which is a feat in a text book; and a credit to the publisher as well as the author.

The book, which is deservingly so popular, is better than ever; and besides the valuable surgical knowledge that it contains it has the value of being most interestingly written; and the many coloured and black and white illustrations are selected with care and are perfectly reproduced. The skiagrams have been selected and printed with great ingenuity; and are of the greatest value and interest because "every picture tells a story."

This book has been described by those who claim to know as the best surgical book in any language; and it is difficult for the less initiated to imagine any better book.

CLEFT LIP AND PALATE.

By W. G. HOLDSWORTH, F.R.C.S.(Edin.), F.R.C.S. (Eng.) London: William Heinemann Medical Books Limited, 1951. 7½" x 9¾", xi plus 126 pp., 87 illustrations. Price: 35s. net.

As a short summary of the history and development of cleft lip and palate surgery and of the many and varied procedures, both primary and secondary, which have been elaborated for their correction, this book must fulfil a useful purpose for ready reference. It does, however, no more than this, and the author makes no particular personal contribution to the subject. It is doubtful whether any surgeon of experience will benefit greatly from its publication, for those who are particularly concerned with this branch of surgery will already have an extensive knowledge of its contents or will prefer to consult the original articles by the various authors to whom reference has been made. On the other hand, it may be of value to the beginner who is looking for a brief outline of the subject, provided he realizes that he will get no critical analysis of the merits or otherwise of the procedures listed.

Within its limits, the book is well produced, the illustrations and drawings are of good quality and easy to follow, and the descriptions of procedure, although in some cases too brief for critical examination, will be readily understood in principle.

WIEDERHERSTELLUNGSCHIRURGIE DES GESICHTS.

By Professor Dr. REINHARD PERWITZSCHKY. Berlin: Walter de Gruyter and Co., 1951. 9¾" x 7½", 228 pp., 176 illustrations.

Wiederherstellungschirurgie Des Gesichts, by Professor Dr. Reinhard Perwitzschky, Director of the Throat, Nose, and Ear Clinic of the one-time German University of Breslau, is the title of a book recently published, printed in German, and dealing with reconstructive surgery of the face. The book is a compendium of the knowledge and experience in this subject which the author gained in World War II when he was in charge of large special hospitals in which it became necessary to house these cases.

The book is limited in its scope, and therefore in its usefulness, in that it does not include injuries of the jaw and of the mouth cavity.

So numerous, so manifold, and so complicated were the face injuries which came under the author's hand that he found little to help him in the standard operations hitherto practised; he had to rely on his knowledge of anatomy, of the principles of the processes of repair and on those governing the management of sepsis, and then use his ingenuity mechanically to repair an injury or make good a facial defect so as to get a satisfactory cosmetic effect.

He has little new to put forward in anaesthesia, an important subject in the technique of facial reconstruction. He does, however, emphasize the particular value in facial surgery of the novocain injection of the Gasserian ganglion, the technique of which was specially perfected by the late Professor Kirschner of Heidelberg. He points out that it causes no shock, can be used in extensive facial injuries, does not distort the tissue like infiltration anaesthesia, and has the advantage over general anaesthesia that it allows a free and clean approach to the wound.

After going through the whole gamut of German synthetic un-absorbable sutures, the author seems to come back to the use of silk.

He adds nothing to the established technique in the use of the pedicled flap; and he falls much short of the English and American methods in his handling of the pre- and post-operative stages in the big facial wounds.

In this book the chief interest lies in its gallery of excellent photographs. Here you find, as you turn over the pages, there are 176 series of pictures, each of which shows the repair steps from the original injury to the finished cosmetic result, and most of which are staged operations which he devised to cope with a particular injury.

ORTHOPAEDIC NURSING.

By MARY POWELL, S.R.N., M.C.S.D. Edinburgh: E. and S. Livingstone Ltd. 8½" x 5¾", xii plus 400 pp., 210 illustrations. Price: 25s. net.

This book has been needed for those who were learning to nurse orthopaedic and fracture patients; and should be a very valuable help. There are many illustrations in this well set out book.